

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
31 March 2005 (31.03.2005)

PCT

(10) International Publication Number
WO 2005/028618 A2

(51) International Patent Classification⁷: C12N

(21) International Application Number:
PCT/US2004/030032

(22) International Filing Date:
15 September 2004 (15.09.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PCT/US2003/029167
15 September 2003 (15.09.2003) US
60/548,789 26 February 2004 (26.02.2004) US

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: IMMUNOGENIC COMPOSITIONS FOR *STREPTOCOCCUS AGALACTIAE*

(57) Abstract: This application relates to Group B Streptococcus ("GBS") vaccines comprising combinations of GBS polypeptide antigens where the polypeptides contribute to the immunological response in a recipient. Preferably, the compositions of the invention comprise a combination of two or more GBS antigens, wherein said combination includes GBS 80 or a fragment thereof. In one embodiment, the combination may consist of two to thirteen GBS antigens selected from an antigen group consisting of GBS 80, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691.



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IMMUNOGENIC COMPOSITIONS FOR *STREPTOCOCCUS AGALACTIAE*

This application claims the benefit and incorporates by reference in its entirety U.S. provisional application 60/548,789, filed February 26, 2004 and claims priority to International Patent Application No. PCT/US03/29167, Attorney Reference No. PP19766.002, filed on September 15, 2003, incorporated herein in its entirety.

FIELD OF THE INVENTION

The invention relates to an immunogenic antigen derived from *Streptococcus agalactiae* ("GBS") and its use in combinations with other GBS antigens to provide for broader coverage among different GBS strains. In particular, the invention relates to a composition comprising a combination of two or more GBS antigens, wherein the combination includes GBS 80 or a fragment thereof. The combination may include GBS 80 and at least one other GBS antigen. For example, the combination may include GBS 80 and up to thirteen GBS antigens. In a preferred embodiment, the combination may include GBS 80 and up to ten GBS antigens. In a more preferred embodiment, the combination may include GBS 80 and up to five GBS antigens. In one embodiment, the combination may consist of two to thirteen GBS antigens selected from an antigen group consisting of GBS 80, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691. Preferably, the combination includes GBS 80 in combination with one or more of GBS 104 and GBS 322.

BACKGROUND OF THE INVENTION

GBS has emerged in the last 20 years as the major cause of neonatal sepsis and meningitis that affect 0.5 – 3 per 1000 live births, and an important cause of morbidity among the older age group affecting 5 – 8 per 100,000 of the population. Current disease management strategies rely on intrapartum antibiotics and neonatal monitoring which have reduced neonatal case mortality from >50% in the 1970's to less than 10% in the 1990's. Nevertheless, there is still considerable morbidity and mortality and the management is expensive. 15 – 35% of pregnant women are asymptomatic carriers and at high risk of transmitting the disease to their babies. Risk of neonatal infection is associated with low serotype specific maternal antibodies and high titers are believed to be protective. In addition, invasive GBS disease is increasingly recognized in elderly adults with underlying disease such as diabetes and cancer.

The "B" in "GBS" refers to the Lancefield classification, which is based on the antigenicity of a carbohydrate which is soluble in dilute acid and called the C carbohydrate. Lancefield identified 13 types of C carbohydrate, designated A to O, that could be serologically differentiated. The organisms

that most commonly infect humans are found in groups A, B, D, and G. Within group B, strains can be divided into at least 9 serotypes (Ia, Ib, Ia/c, II, III, IV, V, VI, VII and VIII) based on the structure of their polysaccharide capsule. In the past, serotypes Ia, Ib, II, and III were equally prevalent in normal vaginal carriage and early onset sepsis in newborns. Type V GBS has emerged as an important cause of GBS infection in the USA, however, and strains of types VI and VIII have become prevalent among Japanese women.

The genome sequence of a serotype V strain 2603 V/R has been published (Ref. 1) and various polypeptides for use as vaccine antigens have been identified (Ref. 2). The vaccines currently in clinical trials, however, are based on polysaccharide antigens. These suffer from serotype-specificity and poor immunogenicity, and so there is a need for effective vaccines against *S. agalactiae* infection.

It is an object of the invention to provide further and improved compositions for providing immunity against GBS disease and/or infection. The compositions are based on a combination of two or more (e.g., three or more) GBS antigens.

SUMMARY OF THE INVENTION

Applicants have discovered that an immunogenic GBS antigen, GBS 80, is particularly suitable for immunization purposes, especially when used in combination with other GBS antigens. The combination may include GBS 80 and at least one other GBS antigen or up to thirteen other GBS antigens. In a preferred embodiment, the combination may include GBS 80 and up to 10 GBS antigens. In a more preferred embodiment, the combination includes GBS 80 and up to five GBS antigens. In particular, the invention relates to a composition comprising a combination of two or more GBS antigens, wherein the combination includes GBS 80 or a fragment thereof. In one embodiment, the combination may consist of two to thirteen GBS antigens selected from the group consisting of GBS 80, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691. Preferably, the combination consists of GBS 80, GBS 104 and GBS 322.

Instead of the full length antigen, the combination may comprise an immunogenic fragment of the selected GBS antigen and/or a polypeptide sequence having sequence identity to the selected antigen.

Preferably, the combination of GBS antigens consists of three, four, five, six, seven, eight, nine, or ten GBS antigens. Still more preferably, the combination of GBS antigens consists of three, four, or five GBS antigens.

DETAILED DESCRIPTION OF THE INVENTION

The practice of the present invention will employ, unless otherwise indicated, conventional methods of chemistry, biochemistry, molecular biology, immunology and pharmacology, within the skill of the art. Such techniques are explained fully in the literature. See, e.g., *Remington's Pharmaceutical Sciences*, Mack Publishing Company, Easton, Pa., 19th Edition (1995); *Methods In Enzymology* (S. Colowick and N. Kaplan, eds., Academic Press, Inc.); and *Handbook of Experimental Immunology*, Vols. I-IV (D.M. Weir and C.C. Blackwell, eds., 1986, Blackwell Scientific Publications); Sambrook, et al., *Molecular Cloning: A Laboratory Manual* (2nd Edition, 1989); *Handbook of Surface and Colloidal Chemistry* (Birdi, K.S. ed., CRC Press, 1997); *Short Protocols in Molecular Biology*, 4th ed. (Ausubel et al. eds., 1999, John Wiley & Sons); *Molecular Biology Techniques: An Intensive Laboratory Course*, (Ream et al., eds., 1998, Academic Press); *PCR (Introduction to Biotechniques Series)*, 2nd ed. (Newton & Graham eds., 1997, Springer Verlag); Peters and Dalrymple, *Fields Virology* (2d ed), Fields et al. (eds.), B.N. Raven Press, New York, NY.

All publications, patents and patent applications cited herein, are hereby incorporated by reference in their entireties.

GBS Antigens

5 As discussed above, the invention provides an immunogenic composition comprising a combination of two or more GBS antigens, wherein said combination includes GBS 80 or a fragment thereof.

10 The combinations of GBS antigens may include polypeptide fragments of the identified GBS antigens. The length of the fragment may vary depending on the amino acid sequence of the specific GBS antigen, but the fragment is preferably at least 7 consecutive amino acids, (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). Preferably the fragment comprises one or more epitopes from the sequence. Other preferred fragments include (1) the N-terminal signal peptides of each identified GBS antigen, (2) the identified GBS antigens without their N-terminal signal peptides, and (3) each identified GBS antigen wherein up to 10 amino acid residues (e.g. 1, 2, 15 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) are deleted from the N-terminus and/or the C-terminus e.g. the N-terminal amino acid residue may be deleted. Other fragments omit one or more domains of the protein (e.g. omission of a signal peptide, of a cytoplasmic domain, of a transmembrane domain, or of an extracellular domain).

20 The combinations of GBS antigens may include polypeptide sequences having sequence identity to the identified GBS antigens. The degree of sequence identity may vary depending on the amino acid sequence (a) in question, but is preferably greater than 50% (e.g. 60%, 65%, 70%, 75%,

80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more). Polypeptides having sequence identity include homologs, orthologs, allelic variants and functional mutants of the identified GBS antigens. Typically, 50% identity or more between two proteins is considered to be an indication of functional equivalence. Identity between proteins is preferably determined by the Smith-Waterman homology search algorithm as implemented in the MPSRCH program (Oxford Molecular), using an affinity gap search with parameters *gap open penalty=12* and *gap extension penalty=1*.

The polypeptides can, of course, be prepared by various means (*e.g.* recombinant expression, purification from GBS, chemical synthesis *etc.*) and in various forms (*e.g.* native, fusions, glycosylated, non-glycosylated *etc.*). They are preferably prepared in substantially pure form (*i.e.* substantially free from other streptococcal or host cell proteins) or substantially isolated form.

GBS 80

As discussed above, the invention relates to the use of GBS 80 in synergistic combination with other GBS antigens. GBS 80 refers to a putative cell wall surface anchor family protein.

Nucleotide and amino acid sequence of GBS 80 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 8779 and SEQ ID 8780. These sequences are also set forth below as SEQ ID NOS 1 and 2:

SEQ ID NO. 1

ATGAAATTATCGAAGAAGTTATTGTTTTTCGGCTGCTGTTTTAAACAATGGTGGCGGGGTCAACTGTTGA
ACCAGTAGCTCAGTTTGCGACTGGAATGAGTATTGTAAGAGCTGCAGAAGTGTCACAAGAACGCCAG
CGAAAACAACAGTAAATATCTATAAATTACAAGCTGATAGTTATAAATCGGAAATTACTTCTAATGGT
GGTATCGAGAATAAAGACGGCGAAGTAAATATCTAACTATGCTAAACTTGGTGACAATGTAAAAGGTTT
GCAAGGTGTACAGTTTAAACGTTATAAAGTCAAGACGGATATTTCTGTTGATGAATTGAAAAAATTGA
CAACAGTTGAAGCAGCAGATGCAAAAAGTTGGAACGATTCTTGAAGAAGGTGTCAGTCTACCTCAAAAA
ACTAATGCTCAAGGTTTGGTCGTCGATGCTCTGGATTCAAAAAGTAATGTGAGATACTTGTATGTAGA
AGATTTAAAGAATTCACCTTCAAACATTACCAAAGCTTATGCTGTACCGTTTGTGTTGGAATTACCAG
TTGCTAACTCTACAGGTACAGGTTTTCCTTTCTGAAATTAATATTTACCCTAAAAACGTTGTAAGTATGAT
GAACCAAAAACAGATAAAGATGTTAAAAAATTAGGTGAGGACGATGCAGGTTATACGATTGGTGAAGA
ATTCAAATGGTTCTTGAAATCTACAATCCCTGCCAATTTAGGTGACTATGAAAAATTTGAAATTACTG
ATAAATTTGCAGATGGCTTGACTTATAAATCTGTTGGAAAAATCAAGATTGGTTGAAAAACACTGAAT
AGAGATGAGCACTACACTATTGATGAACCAACAGTTGATAACCAAAATACATTAAAAAATTACGTTTAA
ACCAGAGAAATTTAAAGAAATTGCTGAGCTACTTAAAGGAATGACCCTTGTTAAAAATCAAGATGCTC
TTGATAAAGCTACTGCAAAATACAGATGATGCGGCATTTTTGGAAATTCCAGTTGCATCAACTATTAAT
GAAAAAGCAGTTTTAGGAAAAGCAATTGAAAATACTTTTGAAGTTCAATATGACCATACTCCTGATAA
AGCTGACAATCCAAAACCATCTAATCCTCCAAGAAAACAGAAAGTTCATACTGGTGGGAAACGATTTG
TAAAGAAAGACTCAACAGAAACACAAACACTAGGTGGTGCTGAGTTTGATTGTTGGCTTCTGATGGG
ACAGCAGTAAATGGACAGATGCTCTTATTAAAGCGAATACTAATAAAAACTATATTGCTGGAGAAGC
TGTTACTGGGCAACCAATCAAATTGAAATCACATACAGACGGTACGTTTGAGATTAAAGGTTTGGCTT
ATGCAGTTGATGCGAATGCAGAGGGTACAGCAGTAACCTACAAATTAAAAGAAACAAAAGCACCAGAA
GGTTATGTAATCCCTGATAAAGAAATCGAGTTTACAGTATCACAAACATCTTATAATACAAAACCAAC
TGACATCACGGTTGATAGTGCTGATGCAACACCTGATACAATTAAAAACAACAAACGTCTTCAATCC
CTAATACTGGTGGTATTGGTACGGCTATCTTTGTCGCTATCGGTGCTGCGGTGATGGCTTTTGCTGTT
AAGGGGATGAAGCGTCGTACAAAAGATAAC

SEQ ID NO: 2

MKLSKKLLFSAAVLTMVAGSTVEPVAQFATGMSIVRAAEVSQERPAKTTVNIYKLQADSYKSEITSNG
 GIENKDGEVISNYAKLGDNVKGLQGVQFKRYKVKTDISVDELKKLTTVEAADAKVGTILEEGVSLPQK
 5 TNAQGLVVDALDSKSNVRYLYVEDLKNSPSNITKAYAVPFVLELPVANSTGTGFLSEINIYPKNVVT
 EPKTDKDVKKLGQDDAGYTI GEEFKWFLKSTIPANLGDYEKFEITDKFADGLTYKSVGKIKIGSKTLN
 RDEHYTIDEPTVDNQNTLKITFKPEKFKEIAELLKGMTLVKNQDALDKATANTDDAAFL EIPVASTIN
 EKAVLGKAIENTFELQYDHTPDKADNPKPSNPPRKPEVHTGGKRFVKKDSTETQTLGGAEFDLLASDG
 10 TAVKWDALIKANTNKNYIAGEAVTGQPIKLKSHTDGTFEIKGLAYAVDANAEGTAVTYKLKETKAPE
 GYVIPDKEIEFTVSQTSYNTKPTDITVDSADATPDTIKNNKRPS IPNTGGIGTAIFVAIGAAMAF
 KGMKRRTKDN

As described above, the combinations of the invention may include a fragment of a GBS
 antigen. In some instances, removal of one or more domains, such as a leader or signal sequence
 15 region, a transmembrane region, a cytoplasmic region or a cell wall anchoring motif, may facilitate
 cloning of the gene encoding the antigen and/or recombinant expression of the GBS protein. In
 addition, fragments comprising immunogenic epitopes of the cited GBS antigens may be used in the
 compositions of the invention.

GBS 80 contains an N-terminal leader or signal sequence region which is indicated by the
 20 underlined sequence at the beginning of SEQ ID NO: 2 above. In one embodiment, one or more
 amino acids from the leader or signal sequence region of GBS 80 are removed. An example of such a
 GBS 80 fragment is set forth below as SEQ ID NO: 3:

SEQ ID NO: 3

AEVSQERPAKTTVNIYKLQADSYKSEITSNGGIENKDGEVISNYAKLGDNVKGLQGVQFKRYKVKT
 25 SVDELKKLTTVEAADAKVGTILEEGVSLPQKTNAQGLVVDALDSKSNVRYLYVEDLKNSPSNITKAYA
 VPFVLELPVANSTGTGFLSEINIYPKNVVTDEPKTDKDVKKLGQDDAGYTI GEEFKWFLKSTIPANLG
 DYEKFEITDKFADGLTYKSVGKIKIGSKTLNRDEHYTIDEPTVDNQNTLKITFKPEKFKEIAELLKGM
 TLVKNQDALDKATANTDDAAFL EIPVASTINEKAVLGKAIENTFELQYDHTPDKADNPKPSNPPRKPE
 30 VHTGGKRFVKKDSTETQTLGGAEFDLLASDGTAVKWDALIKANTNKNYIAGEAVTGQPIKLKSHTDG
 TFEIKGLAYAVDANAEGTAVTYKLKETKAPEGYVIPDKEIEFTVSQTSYNTKPTDITVDSADATPDTI
 KNNKRPS IPNTGGIGTAIFVAIGAAMAFAVKGMKRRTKDN

GBS 80 contains a C-terminal transmembrane region which is indicated by the underlined
 35 sequence near the end of SEQ ID NO: 2 above. In one embodiment, one or more amino acids from
 the transmembrane region and/or a cytoplasmic region are removed. An example of such a GBS 80
 fragment is set forth below as SEQ ID NO: 4:

SEQ ID NO: 4

MKLSKKLLFSAAVLTMVAGSTVEPVAQFATGMSIVRAAEVSQERPAKTTVNIYKLQADSYKSEITSNG
 40 GIENKDGEVISNYAKLGDNVKGLQGVQFKRYKVKTDISVDELKKLTTVEAADAKVGTILEEGVSLPQK
 TNAQGLVVDALDSKSNVRYLYVEDLKNSPSNITKAYAVPFVLELPVANSTGTGFLSEINIYPKNVVT
 EPKTDKDVKKLGQDDAGYTI GEEFKWFLKSTIPANLGDYEKFEITDKFADGLTYKSVGKIKIGSKTLN
 RDEHYTIDEPTVDNQNTLKITFKPEKFKEIAELLKGMTLVKNQDALDKATANTDDAAFL EIPVASTIN
 45 EKAVLGKAIENTFELQYDHTPDKADNPKPSNPPRKPEVHTGGKRFVKKDSTETQTLGGAEFDLLASDG

GBS 80 contains an amino acid motif indicative of a cell wall anchor: **SEQ ID NO: 5**

10

15

20

25 In one embodiment, the leader or signal sequence region, the transmembrane and cytoplasmic regions and the cell wall anchor motif are removed from the GBS 80 sequence. An example of such a GBS 80 fragment is set forth below as SEQ ID NO: 7.

30 AEVSQPERAKTTVNIYKLQADSYKSEITSNGGIENKDGEEVISNYAKLGDNVKGLQGVQFKRYKVKTDI
SVDELKKLTTVEAADAQVGTILEEGVSLPQKTNAQGLVVDALDSKSNVRYLYVEDLKNSPSNITKAYA
VPFVLELPPVANSTGTGFLSEINIYPKNVVTDEPKTKDKDVKKLGQDDAGYTIGEEFKWFLKSTIPANLG
DYEKFEITDKFADGLTYKSVGKIKIGSKTLNRDEHYTTIDEPTVDNQNTLKITFKPEKFKEIAELLKGM
TLVKNQDALDKATANTDDAAFLAIPVASTINEKAVLGKAIENFELQYDHTPDKADNPKPSNPPRKPE
35 VHTGGKRFRVKKDSTETQTLGGAEFDLLASDGTAVKWTDALIKANTNKNYIAGEAVTGQPIKLKSHTDG
TFEIKGLAYAVDANAEGTAVTYKLKETKAPEGYVIPDKEIEFTVSQTSYNTKPTDITVDSADATPDTI
KNNKRPS

40

SEQ ID NO: 2

MKLSKKLLFSAAVLTMVAGSTVEPVAQFATGMSIVRAAEVSQERPAKTTVNIYKLQADSYKSEITSNG
 GIENKDGEVISNYAKLGDNVKGLQGVQFKRYKVKTDISVDELKKLTTVEAADAKVGTILEEGVSLPQK
 5 TNAQGLVVDALDSKSNVRYLYVEDLKNSPSNITKAYAVPFVLELPVANSTGTGFLSEINIYPKNVVTD
 EPKTDKDVKKLGQDDAGYTIGEEFKWFLKSTIPANLGDYEKFEITDKFADGLTYKSVGKIKIGSKTLN
 RDEHYTIDEPTVDNQNLTITFKPEKFKEIAELLKGMTLVKNQDALDKATANTDDAAFLEIPVASTIN
 EKAVLGKAIENFELQYDHTPDKADNPKNPNPPRKPEVHTGGKRFVKKDSTETQTLGGAEFDLLASDG
 TAVKWTDALIKANTNKNYIAGEAVTGQPIKLKSHTDGTFEIKGLAYAVDANAEGTAVTYKCLKETKAPE
 10 GYVIPDKEIEFTVSQTSYNTKPTDITVDSADATPDTIKNNKRPSIPNTGGIGITAI FVAIGAAMAFV
 KGMKRRTKDN

SEQ ID NO: 8

AEVSQERPAKTTVNIYKLQADSYKSEITSNGGIENKDGEVISNYAKLGDNVKGLQGVQFKRYKVKTDI
 15 SVDELKKLTTVEAADAKVGTILEEGVSLPQKTNAQGLVVDALDSKSNVRYLYVEDLKNSPSNITKAYA
 VPFVLELPVANSTGTGFLSEINIYPKNVVTDEPKTDKDVKKLGQDDAGYTIGEEFKWFLKSTIPANLG
 DYEKFEITDKFADGLTYKSVGKIKIGSKTLNRDEHYTIDEPTVDNQNLTITFKPEKFKEIAELLKG

The immunogenicity of the protein encoded by SEQ ID NO: 7 was compared against PBS,
 20 GBS whole cell, GBS 80 (full length) and another fragment of GBS 80, located closer to the C-
 terminus of the peptide (SEQ ID NO: 9, below).

SEQ ID NO: 9

MTLVKNQDALDKATANTDDAAFLEIPVASTINEKAVLGKAIENFELQYDHTPDKADNPKNPNPPRKPEVHTGGK
 RFVKKDSTETQTLGGAEFDLLASDGTAVKWTDALIKANTNKNYIAGEAVTGQPIKLKSHTDGTFEIKGLAYAVDA
 25 NAEGTAVTYKCLKETKAPEGYVIPDKEIEFTVSQTSYNTKPTDITVDSADATPDTIKNNKRPS

Both an Active Maternal Immunization Assay and a Passive Maternal Immunization Assay
 were conducted on this collection of proteins.

As used herein, an Active Maternal Immunization assay refers to an *in vivo* protection assay
 30 where female mice are immunized with the test antigen composition. The female mice are then bred
 and their pups are challenged with a lethal dose of GBS. Serum titers of the female mice during the
 immunization schedule are measured as well as the survival time of the pups after challenge.

Specifically, the Active Maternal Immunization assays referred to herein used groups of four
 CD-1 female mice (Charles River Laboratories, Calco Italy). These mice were immunized
 35 intraperitoneally with the selected proteins in Freund's adjuvant at days 1, 21 and 35, prior to
 breeding. 6-8 weeks old mice received 20 µg protein/dose when immunized with a single
 antigen, 30-45 µg protein/dose (15 µg each antigen) when immunized with combination of
 antigens. The immune response of the dams was monitored by using serum samples taken on day
 0 and 49. The female mice were bred 2-7 days after the last immunization (at approximately t=
 40 36 – 37), and typically had a gestation period of 21 days. Within 48 hours of birth, the pups were
 challenged via I.P. with GBS in a dose approximately equal to an amount which would be
 sufficient to kill 70 – 90 % of unimmunized pups (as determined by empirical data gathered from

PBS control groups). The GBS challenge dose is preferably administered in 50µl of THB medium. Preferably, the pup challenge takes place at 56 to 61 days after the first immunization. The challenge inocula were prepared starting from frozen cultures diluted to the appropriate concentration with THB prior to use. Survival of pups was monitored for 5 days after challenge.

As used herein, the Passive Maternal Immunization Assay refers to an *in vivo* protection assay where pregnant mice are passively immunized by injecting rabbit immune sera (or control sera) approximately 2 days before delivery. The pups are then challenged with a lethal dose of GBS.

Specifically, the Passive Maternal Immunization Assay referred to herein used groups of pregnant CD1 mice which were passively immunized by injecting 1 ml of rabbit immune sera or control sera via I.P., 2 days before delivery. Newborn mice (24-48 hrs after birth) are challenged via I.P. with a 70 - 90% lethal dose of GBS serotype III COH1. The challenge dose, obtained by diluting a frozen mid log phase culture, was administered in 50µl of THB medium.

For both assays, the number of pups surviving GBS infection was assessed every 12 hrs for 4 days. Statistical significance was estimated by Fisher's exact test.

The results of each assay for immunization with SEQ ID NO: 7, SEQ ID NO: 8, PBS and GBS whole cell are set forth in Tables 1 and 2 below.

TABLE 1: Active Maternal Immunization

Antigen	Alive/total	%Survival	Fisher's exact test
PBS (neg control)	13/80	16%	
GBS (whole cell)	54/65	83%	P<0.00000001
GBS80 (intact)	62/70	88%	P<0.00000001
GBS80 (fragment) SEQ ID 7	35/64	55%	P=0.0000013
GBS80 (fragment) SEQ ID 8	13/67	19%	P=0.66

Table 2: Passive Maternal Immunization

Antigen	Alive/total	%Survival	Fisher's exact test
PBS (neg control)	12/42	28%	
GBS (whole cell)	48/52	92%	P<0.00000001
GBS80 (intact)	48/55	87%	P<0.00000001
GBS80 (fragment) SEQ ID 7	45/57	79%	P=0.0000006
GBS80 (fragment) SEQ ID 8	13/54	24%	P=1

As shown in Tables 1 and 2, immunization with the SEQ ID NO: 7 GBS 80 fragment provided a substantially improved survival rate for the challenged pups than the comparison SEQ ID NO: 8 GBS 80 fragment. These results indicate that the SEQ ID NO: 7 GBS 80 fragment may comprise an important immunogenic epitope of GBS 80.

Combinations including GBS 80

The invention includes combinations of two or more GBS antigens wherein the combination includes GBS 80 or a fragment thereof. Applicants have discovered that GBS 80 is particularly suitable for immunization in combination with other GBS antigens and that these antigen combinations provide for a broader coverage among different GBS strains.

Preferably, the combination of GBS antigens consists of three, four, five, six, seven, eight, nine, or ten GBS antigens. Still more preferably, the combination of GBS antigens consists of three, four, or five GBS antigens.

Preferably, the combinations of the invention provide for improved immunogenicity over the immunogenicity of the antigens when administered alone. Improved immunogenicity may be measured, for example, by the Active Maternal Immunization Assay. As discussed above, this assay may be used to measure serum titers of the female mice during the immunization schedule as well as the survival time of the pups after challenge. Preferably, immunization with the immunogenic compositions of the invention yield an increase of at least 2 percentage points (preferably at least 3, 4 or 5 percentage points) in the percent survival of the challenged pups as compared to the percent survival from maternal immunization with a single antigen of the composition when administered alone. Preferably, the increase is at least 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 percentage points. Preferably, the GBS combinations of the invention comprising GBS 80 demonstrate an increase in the percent survival as compared to the percent survival from immunization with a non-GBS 80 antigen alone.

According to one embodiment of the invention, combinations of antigens or fusion proteins containing a portion or portions of the antigens will include GBS 80 or a portion thereof in combination with from one to 10 antigens, preferably one to 10 or less antigens. Such other antigens include by way of example and not limitation, GBS 67, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691. Still other antigens are identified in U.S. Serial Number 10/415,182, filed April 28, 2003, hereby incorporated in its entirety.

Combinations, for example, can include GBS 80, GBS 104, GBS 322, and GBS 276, ; GBS 80, GBS 338, GBS 330; GBS 80, GBS 330, GBS 104; GBS 80, GBS 104, GBS 404; GBS 80, GBS 338, GBS 104; GBS 80, GBS 338, GBS 404; GBS 338, GBS 330, GBS 104; GBS 338, GBS 104, GBS 404; GBS 80, GBS 330, GBS 404; GBS 80, GBS 322, GBS 104; GBS 80, GBS 322, GBS 276; GBS 80, GBS 322, GBS 91; GBS 80, GBS 104, GBS 276; GBS 80, GBS 104, GBS 91; GBS 80, GBS 276, GBS 91; GBS 80, GBS 322, GBS 104; GBS 80, GBS 322, GBS 276; GBS 80, GBS 322, GBS 91; GBS 80, GBS 104, GBS 276; GBS 80, GBS 104, GBS 91; GBS 80, GBS 276, GBS 91; GBS 80, GBS 690, GBS 691; GBS 80, GBS 690, GBS 338; GBS 80, GBS 690, GBS 305; GBS 80, GBS 691,

GBS 305; GBS 80, GBS 338, GBS 305; GBS 80, GBS 338, GBS 361; GBS 80, GBS 305, GBS 361; GBS 80, GBS 184, GBS 691; GBS 80, GBS 691, GBS 338; GBS 80, GBS 104, GBS 276, GBS 322; GBS 80, GBS 104, GBS 67, and GBS 322. Examples of combinations of the invention which demonstrate improved immunogenicity are set forth below. A more detailed description of the GBS antigens referred to in these experiments is set forth following the examples.

EXAMPLE 1: Active Maternal Immunization Assay of GBS 80 alone vs. in combination

In this example, the Active Maternal Immunization Assay was used to measure the percent survival of pups challenged with a Type III serotype of GBS (COH1 isolate), at t=56 days. The maternal mice were immunized according to the Active Maternal Immunization Assay schedule discussed above with GBS 80 alone, combinations of GBS antigens (with and without GBS 80), placebo (PBS) or inactivated whole cell GBS isolate as indicated in Table 3 below. In these experiments, the challenge dose for GBS Type III, strain isolate COH1 sufficient to kill 70 – 90 % of unimmunized pups is approximately equal to 10 x LD 50% (where LD 50% is the statistically derived Median Lethal Dose).

Table 3: Active Maternal Immunization Assay of GBS 80 alone vs. in combination

α -GBS	I Challenge t=56 days Type III COH1 10 x LD 50%	
	Alive/treated	Survival %
α -PBS	3/26	11
α -GBS III	9/20	45
80	24/34	70
80+338+330	39/40	97
80+330+104	38/40	95
80+104+404	24/24	100
80+338+104	33/34	97
80+338+404	30/30	100
338+330+104	22/30	73
338+104+404	24/37	65
80+330+404	25/28	89

As shown in Table 3, combinations of GBS antigens which included GBS 80 demonstrated an improved immunogenicity over the use of the antigens alone. For example, immunization with GBS 80 alone yielded a 70% survival rate among the challenged pups. Immunization with combinations of GBS 80 with GBS 338, GBS 330, GBS 104, and GBS 404 yielded 95 to 100% survival rate among the challenged pups. This is an increase of 25 to 30 percentage points.

By comparison, combinations of these antigens which did not include GBS 80 failed to achieve the % survival of GBS 80 alone. For example, immunization with GBS 338, GBS 104 and

GBS 404 yielded a 65% survival rate. Replacement of any one of these antigens with GBS 80 dramatically increased the percent survival rate to between 97 and 100%. This is an increase of 32 to 35 percentage points. (See percent survival rates of GBS 80, 338, 101 (97%); GBS 80, 338, 404 (100%) and GBS 80, 104, 404 (100%)). Similarly, immunization with GBS 338, 330 and 104 yielded a 73% survival rate. Replacement of any one of these antigens with GBS 80 increased the percent survival rate to between 95 – 97%.

These findings indicate that protection from COH1 isolate is increased with use of GBS 80 in combination with other GBS antigens.

EXAMPLE 2: Active Maternal Immunization Assay of GBS 80, GBS 322, GBS 276, GBS 104 alone vs. in combination

In this example, the Active Maternal Immunization Assay was used to measure the percent survival of pups challenged with a Type III serotype of GBS (COH1 isolate) at t=56 days. The maternal mice were immunized according to the Active Maternal Immunization Assay schedule discussed above with a single GBS antigen, combinations of GBS antigens with GBS 80, and placebo (PBS) as indicated in Table 4 below.

Table 4: Active Maternal Immunization Assay of GBS 80, GBS 322, GBS 276 or GBS 104 alone vs. in combination with GBS 80

α -GBS	I Challenge t=56 days Type III COH1 10x LD 50%	
	Alive/treated	Survival %
80 + 322 + 104	27/27	100
80 + 322 + 276	35/38	92
80 + 322 + 91	24/24	100
80 + 104 + 276	29/30	97
80 + 104 + 91	36/40	90
80 + 276 + 91	33/40	82
GBS 80	24/30	80
GBS 322	7/40	17
GBS 276	13/37	35
GBS 104	28/38	74
α -PBS	2/27	7

As shown in Table 4, the combinations of the antigens with GBS 80 yielded improved immunogenicity over the use of the antigens alone. For example, immunization with GBS 322 alone yielded a 17 % survival rate among the challenged pups. Immunization with combinations of GBS 322 with GBS 80 and another GBS antigen yielded survival rates of 92 – 100%. As another example, immunization with GBS 104 alone yielded a 74% survival rate. Immunization with combinations of

GBS 104 with GBS 80 and another GBS antigen yielded survival rates of 90 – 100%. As another example, immunization with GBS 276 alone yielded a 35% survival rate. Immunization with combinations of GBS 276 with GBS 80 and another GBS antigen yielded survival rates of 82 – 97%.

Having demonstrated the immunogenicity of the above-described combinations, the duration of the immune response in the mouse model was further analysed. The maternal mice used in the above described Active Maternal Immunization Assay were mated a second time and the resulting pups challenged with a different GBS serotype (Type V, CJB 111 isolate) at a dramatically higher dose (300x LD 50%) at t=91 days. The parameters of this second, much stronger challenge were outside those of the standard Active Maternal Immunization Assay and were meant to probe the limits of the immunological memory generated from the original maternal immunization in the mouse model. Indication of immunological memory in this model under these conditions is thought to be significant. As shown in Table 5, even under these extreme conditions, increased survival rates were generally achieved, particularly for the combination comprising GBS 80, GBS 322 and GBS 104. It was surprising to note that the percent survival rate for the combination of GBS 80, GBS 233 and GBS 104 was 100% for both the first and second challenges.

Table 5: Second generation pups challenged with higher dose of different strain

α -GBS	II Challenge t=91 days Type V CJB111 300x LD 50%	
	Alive/treated	Survival %
80 + 322 + 104	20/20	100
80 + 322 + 276	32/37	86
80 + 322 + 91	27/30	90
80 + 104 + 276	22/37	59
80 + 104 + 91	36/39	92
80 + 276 + 91	23/28	82
GBS 80	13/30	43
GBS 322	25/30	83
GBS 276	18/40	45
GBS 104	21/39	54
α -PBS	9/36	25

EXAMPLE 3: Active Maternal Immunization Assay of combinations of GBS 80 with GBS 690, GBS 691, GBS 338, GBS 305, GBS 361 and GBS 184

In this example additional combinations of GBS antigens were used in the Active Maternal Immunization Assay, again with a GBS Type III COH1 isolate challenge. The maternal mice were immunized according to the Active Maternal Immunization Assay schedule described above with the combinations of GBS antigens set forth in Table 6 below.

Table 6: Active Maternal Immunization Assay using combinations of GBS 80 with GBS 690, GBS 691, GBS 338, GBS 305, GBS 361 and GBS 184

α -GBS	I Challenge t=56 days Type III COH1 10x LD 50%	
	Alive/treated	Survival %
80 + 690 + 691	26/29	90
80 + 690 + 338	35/40	87
80 + 690 + 305	34/35	97
80 + 691 + 305	37/40	92
80 + 338 + 305	25/30	83
80 + 338 + 361	26/30	87
80 + 305 + 361	23/30	77
80 + 184 + 691	32/39	82
α -PBS	10/40	25

5 The maternal mice in this model were also mated a second time and the resulting pups challenged with the same GBS isolate at a dramatically higher dose (100x LD 50%) at t=84 days. As in the example above, the parameters of this second, much stronger challenge were outside those of the standard Active Maternal Immunization Assay and were meant to probe the limits of the immunological memory generated from the original maternal immunization in the mouse model. As shown in Table 7, even under these extreme conditions, some of the survival rates remained at or above 70%. Surprisingly, the percent survival rates for the combination of GBS 80, GBS 184 and GBS 691 actually increased.

Table 7: Second generation pups challenged with higher dose

α -GBS	II Challenge t=84 days Type III COH1 100x LD 50%	
	Alive/treated	Survival %
80 + 690 + 691	19/39	49
80 + 690 + 338	21/30	70
80 + 690 + 305	23/40	57
80 + 691 + 305	22/30	73
80 + 338 + 305	18/30	60
80 + 338 + 361	25/40	62
80 + 305 + 361	21/30	70
80 + 184 + 691	35/40	87
α -PBS	4/20	20

EXAMPLE 4: Active Maternal Immunization Assay using combinations of GBS 80 with GBS 690, GBS 691, GBS 338, GBS 305, and GBS 361

In this example additional combinations of GBS antigens were used in the Active Maternal

- 5 Immunization Assay, this time with a GBS Type V, CJB111 isolate challenge. In these experiments, the challenge dose for the GBS Type V, CJB111 isolate sufficient to kill 70 – 90% of unimmunized pups is approximately equal to 60 x LD 50% (where LD 50% is the statistically derived Median Lethal Dose). The maternal mice were immunized according to the Active Maternal Immunization Assay schedule described above with the combinations of GBS antigens set forth in Table 8 below.
- 10 As shown in Table 8, in this particular challenge study with this specific Type V strain isolate, the survival rates for all of the combinations achieved at least 70%.

Table 8: Active Maternal Immunization Assay using combinations of GBS 80 with GBS 690, GBS 691, GBS 338, GBS 305 and GBS 361

α -GBS	I Challenge t=56 days	
	Type V CJB111 60x LD 50%	
	Alive/treated	Survival %
80 + 690 + 691	24/30	80
80 + 690 + 338	11/17	70
80 + 691 + 338	7/10	70
80 + 691 + 305	21/30	70
80 + 338 + 305	26/30	87
80 + 338 + 361	26/30	87
80 + 305 + 361	28/30	93
GBS 80	21/30	70
α -PBS	5/18	28

15

- The maternal mice in this model were also mated a second time and the resulting pups challenged with the same GBS isolate at a dramatically higher dose (600x LD 50%) at t=84 days. As in the example above, the parameters of this second, much stronger challenge were outside those of the standard Active Maternal Immunization Assay and were meant to probe the limits of the
- 20 immunological memory generated from the original maternal immunization in the mouse model. As shown in Table 9, even under these extreme conditions, some of the survival rates remained above 70%. Surprisingly, the percent survival for two of the antigen groups actually increased (GBS 80, GBS 690 and GBS 338) and (GBS 80, GBS 691 and GBS 338).

Table 9: Second generation pups challenged with higher dose

α -GBS	II Challenge t=84 days	
	Type V CJB111 600x LD 50%	
	Alive/treated	Survival %
80 + 690 + 691	27/37	73
80 + 690 + 338	15/20	75
80 + 691 + 338	27/30	90
80 + 691 + 305	23/40	57
80 + 338 + 305	12/20	60
80 + 338 + 361	24/30	80
80 + 305 + 361	24/30	80
GBS 80	24/30	80
α -PBS	ND	ND

EXAMPLE 5: Active Maternal Immunization Assay using combinations of GBS 80 with GBS 104, GBS 276, and GBS 322

In this example an additional combination of GBS antigens was used in the Active Maternal Immunization Assay, this time with an isolate challenge of different GBS strains. In these experiments, the challenge dose for the different GBS strains was sufficient to kill 60 – 90% of unimmunized pups and is equal to 10 x LD 50% (where LD 50% is the statistically derived Median Lethal Dose). The maternal mice were immunized according to the Active Maternal Immunization Assay schedule described above with the combination of GBS 80 antigen with GBS 104, GBS 276, and GBS 322 antigens in the GBS strains set forth in Table 10 below. Survival % was observed with the GBS combination with two different adjuvants, Alum and Freund's. As shown in Tables 10 and 11, in this particular challenge study, the survival rates for the combination in all of the GBS strains achieved up to 96%.

Table 10: Active Maternal Immunization Assay using combinations of GBS 80 with GBS 104, GBS 276, and GBS 322 – Alum adjuvant

ALUM					
Mix=322+80+104+276				PBS	
GBS strains	Type	Alive/treated	Survival %	Alive/treated	Survival %
JM9130013	VIII	32/36	89	18/46	40
CJB111	V	118/145	81	21/110	19
COH1	III	96/115	83	22/104	21
M781	III	42/52	81	18/48	38
2603	V	79/145	54	28/128	22
18RS21	II	86/186	46	24/131	18
DK21	II	31/140	22	28/118	24
7357b –	Ib	25/88	28	25/106	23
A909	Ia	4/40	10	9/60	15
090	Ia	2/31	6	4/53	7
SMO53	VII	17/54	31	4/39	10

5

Table 11: Active Maternal Immunization Assay using combinations of GBS 80 with GBS 104, GBS 276, and GBS 322 – Freund adjuvant

Freund					
Mix=322+80+104+276				PBS	
GBS strains	Type	Alive/treated	Survival %	Alive/treated	Survival %
JM9130013	VIII	nd	nd	nd	nd
CJB111	V	47/49	96	12/46	26
COH1	III	47/50	94	12/50	24
M781	III	33/50	66	6/50	12
2603	V	28/30	93	8/48	17
18RS21	II	31/78	40	10/46	22
DK21	II	37/68	54	15/60	25
H36B	Ib	8/38	21	5/60	8
7357b –	Ib	29/50	58	5/50	10
A909	Ia	18/49	37	6/49	12

Accordingly, the invention therefore includes compositions comprising combinations of two or more GBS antigens, wherein the combination includes GBS 80 or a fragment thereof or a polypeptide sequence having sequence identity thereto.

10

In one embodiment, the combination may consist of two to thirteen GBS antigens, including GBS 80. As an example, the combination may contain GBS 80 and other GBS antigens selected from the group consisting of GBS 80, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691. Preferably, the combination includes

GBS 80 in combination with one or more of GBS 104 and GBS 322. For example, the combination may include GBS 80, GBS 104, GBS 322 and GBS 67.

Instead of the full length antigen, the combination may comprise an immunogenic fragment of the selected GBS antigen and/or a polypeptide sequence having sequence identity to the selected antigen.

Preferably, the combination of GBS antigens consists of three, four, five, six, seven, eight, nine, or ten GBS antigens. Still more preferably, the combination of GBS antigens consists of three, four, or five GBS antigens.

Details of examples of GBS antigens for use in combination with GBS 80 are set forth below.

GBS 91

GBS 91 refers to a GBS C3 binding polypeptide. Nucleotide and amino acid sequences of GBS 91 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 8937 and SEQ ID 8938. These sequences are set forth below as SEQ ID NOS 10 and 11:

SEQ ID NO. 10

ATGAAAAAAGGACAAGTAAATGATACTAAGCAATCTTACTCTCTACGTAAATATAAATTTGGTTTAGC
ATCAGTAATTTTAGGGTCATTCATAATGGTCACAAGTCCTGTTTTTGC GGATCAAAC TACATCGGTTTC
AAGTTAATAATCAGACAGGCACTAGTGTGGATGCTAATAATTCCTTCCAATGAGACAAGTGC GTCAAGT
GTGATTACTTCCAATAATGATAGTGTTCAAGCGTCTGATAAAGTTGTAAATAGTCAAATAACGGCAAC
AAAGGACATTACTACTCCTTTAGTAGAGACAAAGCCAATGGTGGAAAAACATTACCTGAACAAGGGA
ATTATGTTTTATAGCAAAGAAACCGAGGTGAAAAATACACCTTCAAATCAGCCCCAGTAGCTTTCTAT
GCAAAGAAAGGTGATAAAGTTTTCTATGACCAAGTATTTAATAAAGATAATGTGAAATGGATTTCATA
TAAGTCTTTTTGTGGCGTACGTCGATACGCAGCTATTGAGTCACTAGATCCATCAGGAGGTTTCAGAGA
CTAAAGCACCTACTCCTGTAACAAATTCAGGAAGCAATAATCAAGAGAAAATAGCAACGCAAGGAAAT
TATACATTTTTCACATAAAGTAGAAGTAAAAATGAAGCTAAGGTAGCGAGTCCAAC TCAATTTACATT
GGACAAAGGAGACAGAATTTTTTACGACCAATACTAATACTATTGAAGGAAATCAGTGGTTATCTTATA
AATCATTTCAATGGTGTTCGTCGTTTTGTTTTGCTAGGTAAAGCATCTTCAGTAGAAAAAACTGAAGAT
AAAGAAAAAGTGTCTCCTCAACCACAAGCCCGTATTACTAAAAGTGGTAGACTGACTATTTCTAACGA
AACAAC TACAGGTTTTGATATTTTAATTACGAATATTAAGATGATAACGGTATCGCTGCTGTTAAGG
TACCGGTTTGGACTGAACAAGGAGGGCAAGATGATATTAAATGGTATACAGCTGTA ACTACTGGGGAT
GGCAACTACAAAGTAGCTGTATCATTTGCTGACCATAAGAATGAGAAGGGTCTTTATAATATTCATTT
ATACTACCAAGAAGCTAGTGGGACACTTGTAGGTGTAACAGGA ACTAAAGTGACAGTAGCTGGA ACTA
ATTCCTTCTCAAGAACCTATTGAAAATGGTTTAGCAAAGACTGGTGT TTATAATATTATCGGAAGTACT
GAAGTAAAAAATGAAGCTAAAATATCAAGTCAGACCCAATTTACTTTAGAAAAAGGTGACAAAATAAA
TTATGATCAAGTATTGACAGCAGATGGTTACCAGTGGATTTCTTACAAATCTTATAGTGGTGTTCGTC
GCTATATTCCTGTGAAAAAGCTAACTACAAGTAGTGAAAAAGCGAAAGATGAGGCGACTAAACCGACT
AGTTATCCCAACTTACCTAAAACAGGTACCTATACATTTACTAAAAGTGTAGATGTGAAAAGTCAACC
TAAAGTATCAAGTCCAGTGGAAATTTAATTTTCAAAGGGTGAAAAAATACATTATGATCAAGTGTTAG
TAGTAGATGGTCATCAGTGGATTTTCATACAAGAGTTATTCCGGTATTTCGTCGCTATATTGAAATT

SEQ ID NO. 11

MKKGQVNDTKQSYSLRKYKFGLASVILGSFIMVTSVPVFADQTTSVQVNNQTGTSVDANNSSNETSASS
VITSNNDVSQASDKVVNSQNTATKDIITPLVETKPMVEKTLPEQGNVYVSKETEVKNTPSKSAPVAFY
AKKGDKVIFYDQVFNKDNVKWISYKSF CGVRRYAAIESLDPSGGSETKAPT PVTNSGSNNQEKIATQGN
YTF SHKVEVKNEAKVASPTQFTLDKGDRIFYDQILITIEGNQWLSYKSFNGVRRFVLLGKASSVEKTED
KEKVSPPQPARITKTGRLTISNETTTGFDILITNIKDDNGIAAVKVPVWTEQGGQDDIKWYTA VTTGD

GNYKVAVSFADHKNEKGLYNIHLYYQEASGTLVGVTGKVTVAGTNSSQEPIENGLAKTGVYNIIGST
 EVKNEAKISSQTQFTLEKGDKINYDQVLTADGYQWISYKSYSGVRRYIPVKKLTTSSSEKAKDEATKPT
SYPNLPKTGTYTFTKTVDVKSQPKVSSPVEFNFQKGEKIHYDQVLVVDGHQWISYKSYSGIRRYIEI

- 5 GBS 91 contains an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO: 11 above. In one embodiment, one or more amino acids from this leader or signal sequence region of GBS 91 are removed. An example of such a GBS 91 fragment is set forth below as SEQ ID NO: 12.

10 **SEQ ID NO: 12**

DQTTSVQVNNQTGTSVDANNSSNETSASSVITSNNDSVQASDKVNSQNTATKDITTPLVETKPMVEK
 TLPEQGNVYVSKETEVEKNTPSKSAPVAFYAKKGDQVFDQVFNKDNVWISYKSYSGVRRYAAIESLD
 PSGGSETKAPTPTVNSGSNNQEKIATQGNITFSHKVEVKNEAKVASPTQFTLDKGDRIFYDQILTIEG
 15 NQWLSYKSFNGVRRFVLLGKASSVEKTEDKEKVSPQPQARITKTGRLTISNETTTGFDILITNIKDDN
 GIAAVKVPVWTEQGGQDDIKWYTAVTTGDGNYKVAVSFADHKNEKGLYNIHLYYQEASGTLVGVTGK
 VTVAGTNSSQEPIENGLAKTGVYNIIGSTEVEKNEAKISSQTQFTLEKGDKINYDQVLTADGYQWISYK
 SYSGVRRYIPVKKLTTSSSEKAKDEATKPTSYPNLPKTGTYTFTKTVDVKSQPKVSSPVEFNFQKGEKI
 HYDQVLVVDGHQWISYKSYSGIRRYIEI

- 20 GBS 91 contains a C-terminal transmembrane region which may be located within the underlined region near the end of SEQ ID NO: 11 above. In one embodiment, one or more amino acids from the transmembrane and cytoplasmic regions are removed. An example of such a GBS 91 fragment is set forth below as SEQ ID NO: 13.

25 **SEQ ID NO: 13**

MKKGQVNDTKQSYSLRKYKFGLASVILGSFIMVTSPVFADQTTSVQVNNQTGTSVDANNSSNETSASS
 VITSNNDSVQASDKVNSQNTATKDITTPLVETKPMVEKTLPEQGNVYVSKETEVEKNTPSKSAPVAFY
 AKKGDQVFDQVFNKDNVWISYKSYSGVRRYAAIESLDPSGGSETKAPTPTVNSGSNNQEKIATQGN
 YTFSHKVEVKNEAKVASPTQFTLDKGDRIFYDQILTIEGNQWLSYKSFNGVRRFVLLGKASSVEKTED
 30 KEKVSPQPQARITKTGRLTISNETTTGFDILITNIKDDNGIAAVKVPVWTEQGGQDDIKWYTAVTTGD
 GNYKVAVSFADHKNEKGLYNIHLYYQEASGTLVGVTGKVTVAGTNSSQEPIENGLAKTGVYNIIGST
 EVKNEAKISSQTQFTLEKGDKINYDQVLTADGYQWISYKSYSGVRRYIPVKKLTTSSSEKAKDEATKPT
 SYPNLPKTG

- 35 GBS 91 contains an amino acid motif indicative of a cell wall anchor: **SEQ ID NO: 14**
 LTKTG (shown in *italics* in SEQ ID NO: 11 above). In one embodiment, both the transmembrane domain and the cell wall anchor motif are removed from GBS 91. An example of such a GBS 91 fragment is set forth below as SEQ ID NO: 15.

40 **SEQ ID NO: 15**

MKKGQVNDTKQSYSLRKYKFGLASVILGSFIMVTSPVFADQTTSVQVNNQTGTSVDANNSSNETSASS
 VITSNNDSVQASDKVNSQNTATKDITTPLVETKPMVEKTLPEQGNVYVSKETEVEKNTPSKSAPVAFY
 AKKGDQVFDQVFNKDNVWISYKSYSGVRRYAAIESLDPSGGSETKAPTPTVNSGSNNQEKIATQGN
 YTFSHKVEVKNEAKVASPTQFTLDKGDRIFYDQILTIEGNQWLSYKSFNGVRRFVLLGKASSVEKTED
 45 KEKVSPQPQARITKTGRLTISNETTTGFDILITNIKDDNGIAAVKVPVWTEQGGQDDIKWYTAVTTGD
 GNYKVAVSFADHKNEKGLYNIHLYYQEASGTLVGVTGKVTVAGTNSSQEPIENGLAKTGVYNIIGST

EVKNEAKISSQTQFTLEKGDKINYDQVLTADGYQWISYKSYSGVRRYIPVKKLTTSSSEKAKDEATKPT
SYPN

In one embodiment, one or more amino acids from the leader or signal sequence region and
one or more amino acids from the transmembrane and cytoplasmic regions are removed from the GBS
91 sequence. An example of such a GBS 91 fragment is set forth below as SEQ ID NO: 16.

SEQ ID NO: 16

DQTTSVQVNNQTGTSVDANSSNETSASSVITSNNDSVQASDKVVNSQNTATKDITPLVETKPMVEK
TLPEQGNVYVSKETEVKNTPSKSAPVAFYAKKGDQVFYDQVFNKDNVWKWISYKSFVCGVRRYAAIESLD
PSGGSETKAPTPTNSGSNNQEKIATQGNVTFSHKVEVKNEAKVASPTQFTLDKGDRIFYDQILTIEG
NQWLSYKSFNGVRRFVLLGKASSVEKTEDKEKVSPQPQARITKTGRLTISNETTTGFDILITNIKDDN
GIAAVKVPVWTEQGGQDDIKWYTAVTTGDGNYKVAVSFADHKNEKGLYNIHLYYQEASGTLVGVTGK
VTVAGTNSSQEPIENGLAKTGVYNIIGSTEVKNEAKISSQTQFTLEKGDKINYDQVLTADGYQWISYK
SYSGVRRYIPVKKLTTSSSEKAKDEATKPTSYPNLPKTG

In another embodiment, the leader or signal sequence region, the transmembrane and
cytoplasmic regions, and the cell wall anchor motif are all removed from the GBS 91 sequence. An
example of such a GBS 91 fragment is set forth below as SEQ ID NO: 17.

SEQ ID NO: 17

DQTTSVQVNNQTGTSVDANSSNETSASSVITSNNDSVQASDKVVNSQNTATKDITPLVETKPMVEK
TLPEQGNVYVSKETEVKNTPSKSAPVAFYAKKGDQVFYDQVFNKDNVWKWISYKSFVCGVRRYAAIESLD
PSGGSETKAPTPTNSGSNNQEKIATQGNVTFSHKVEVKNEAKVASPTQFTLDKGDRIFYDQILTIEG
NQWLSYKSFNGVRRFVLLGKASSVEKTEDKEKVSPQPQARITKTGRLTISNETTTGFDILITNIKDDN
GIAAVKVPVWTEQGGQDDIKWYTAVTTGDGNYKVAVSFADHKNEKGLYNIHLYYQEASGTLVGVTGK
VTVAGTNSSQEPIENGLAKTGVYNIIGSTEVKNEAKISSQTQFTLEKGDKINYDQVLTADGYQWISYK
SYSGVRRYIPVKKLTTSSSEKAKDEATKPTSYPN

Further information regarding GBS 91 can be found in WO 01/25440 (C3 binding
polypeptide), WO 01/32882 (ID-65), WO 02/31156 (BVH) and Reinscheid et al., *Microbiology*
(2002) 148: 3245-3254 (*bsp* gene), each of which are incorporated herein by reference in their
entirety.

GBS 104

GBS 104 refers to a putative cell wall surface anchor family protein. It has been referred to as
emaA protein. Nucleotide and amino acid sequences of GBS 104 sequenced from serotype V isolated
strain 2603 V/R are set forth in Ref. 2 as SEQ ID 8777 and SEQ ID 8778. These sequences are set
forth below as SEQ ID NOS 18 and 19:

SEQ ID NO. 18

ATGAAAAAGAGACAAAAAATATGGAGAGGGTTATCAGTTACTTTACTAATCCTGTCCCAAATTCATT
TGGTATATTGGTACAAGGTGAAACCCAAGATACCAATCAAGCACTTGAAAAAGTAATTGTTAAAAAA
5 C GGGAGACAATGCTACACCATTAGGCAAAGCGACTTTTGTGTTAAAAAATGACAATGATAAGTCAGAA
ACAAGTCACGAAACGGTAGAGGGTCTGGAGAAGCAACCTTTGAAAACATAAAACCTGGAGACTACAC
ATTAAGAGAAGAAACAGCACCAATTGGTTATAAAAAAACTGATAAAACCTGGAAAGTTAAAGTTGCAG
ATAACGGAGCAACAATAATCGAGGGTATGGATGCAGATAAAGCAGAGAAACGAAAAGAAGTTTTGAAT
10 G C C C A A T A T C C A A A A T C A G C T A T T T A T G A G G A T A C A A A G A A A A T T A C C C A T T A G T T A A T G T A G A G G G
T T C C A A A G T T G G T G A A C A A T A C A A G C A T T G A A T C C A A T A A A T G G A A A G A T G G T C G A A G A G A G A T T G
C T G A A G G T T G G T T A T C A A A A A A A A T T A C A G G G G T C A A T G A T C T C G A T A A G A A T A A A T A T A A A A T T G A A
T T A A C T G T T G A G G G T A A A A C C A C T G T T G A A A C G A A A G A A C T T A A T C A A C C A C T A G A T G T C G T T G T G C T
A T T A G A T A A T T C A A A T A G T A T G A A T A A T G A A A G A G C C A A T A A T T C T C A A A G A G C A T T A A A A G C T G G G G
15 A A G C A G T T G A A A A G C T G A T T G A T A A A A T T A C A T C A A A T A A A G A C A A T A G A G T A G C T C T T G T G A C A T A T
G C C T C A A C C A T T T T T G A T G G T A C T G A A G C G A C C G T A T C A A A G G G A G T T G C C G A T C A A A A T G G T A A A G C
G C T G A A T G A T A G T G T A T C A T G G G A T T A T C A T A A A A C T A C T T T T A C A G C A A C T A C A C A T A A T T A C A G T T
A T T T A A A T T T A C A A A T G A T G C T A A C G A A G T T A A T A T T C T A A A G T C A A G A A T T C C A A A G G A A G C G G A G
C A T A T A A A T G G G G A T C G C A C G C T C T A T C A A T T T G G T G C G A C A T T T A C T C A A A A G C T C T A A T G A A A G C
A A A T G A A A T T T T A G A G A C A C A A A G T T C T A A T G C T A G A A A A A A C T T A T T T T T C A C G T A A C T G A T G G T G
20 T C C C T A C G A T G T C T T A T G C C A T A A A T T T T A A T C C T T A T A T A T C A A C A T C T T A C C A A A A C C A G T T T A A T
T C T T T T T T A A A T A A A A T A C C A G A T A G A A G T G G T A T T C T C C A A G A G G A T T T T A T A A T C A A T G G T G A T G A
T T A T C A A A T A G T A A A A G G A G A T G G A G A G A G T T T T A A A C T G T T T T C G G A T A G A A A G T T C C T G T T A C T G
G A G G A A C G A C A C A A G C A G C T T A T C G A G T A C C G C A A A A T C A A C T C T C T G T A A T G A G T A A T G A G G G A T A T
G C A A T T A A T A G T G G A T A T A T T T A T C T C T A T T G G A G A G A T T A C A A C T G G G T C T A T C C A T T T G A T C C T A A
25 G A C A A A G A A A G T T T C T G C A A C G A A A C A A A T C A A A C T C A T G G T G A G C C A A C A C A T T A T A C T T T A A T G
G A A A T A T A A G A C C T A A A G G T T A T G A C A T T T T T A C T G T T G G G A T T G G T G T A A A C G G A G A T C C T G G T G C A
A C T C C T C T T G A A G C T G A G A A A T T A T G C A A T C A A T A T C A A G T A A A A C A G A A A A T T A T A C T A A T G T T G A
T G A T A C A A A T A A A A T T A T G A T G A G C T A A A T A A A T A C T T T A A A A C A A T T G T T G A G G A A A A C A T T C T A
T T G T T G A T G G A A A T G T G A C T G A T C C T A T G G G A G A G A T G A T T G A A T T C C A A T T A A A A A T G G T C A A A G T
30 T T T A C A C A T G A T G A T T A C G T T T T G G T T G G A A A T G A T G G C A G T C A A T T A A A A A A T G G T G T G G C T C T T G G
T G G A C C A A A C A G T G A T G G G G G A A T T T T A A A A G A T G T T A C A G T G A C T T A T G A T A A G A C A T C T C A A C C A
T C A A A A T C A A T C A T T T G A A C T T A G G A A G T G G A C A A A A A G T A G T T C T T A C C T A T G A T G T A C G T T T A A A A
G A T A A C T A T A T A G T A A C A A A T T T A C A A T A C A A A T A A T C G T A C A A C G C T A A G T C C G A A G A G T G A A A A
A G A A C C A A A T A C T A A T C G T G A T T T C C C A A A T T C C G T G A T G T T C G T G A G T T T C C G G T A C T A A
35 C C A T C A G T A A T C A G A A G A A A A T G G G T G A G G T G A A T T A T T A A A G T T A A T A A A G A C A A A C A T T C A G A A
T C G C T T T T G G G A G C T A A G T T T C A A C T T C A G A T A G A A A A A G A T T T T T C T G G G T A T A G C A A T T T G T T C C
A G A G G G A A G T G A T G T T A C A C A A A G A A T G A T G G T A A A A T T A T T T T A A A G C A C T T C A A G A T T G T A A C T
A T A A A T T A T A T G A A A T T T C A A G T C C A G A T G G C T A T A T A G A G G T T A A A A C G A A A C C T G T T G T G C A T T T
A C A A T T C A A A A T G G A G A A G T T A C G A A C C T G A A A G C A G A T C C A A A T G C T A A T A A A A T C A A A T C G G G T A
40 T C T T G A A G G A A A T G G T A A A C A T C T T A T T A C C A A C A C T C C C A A A C G C C C A C C A G G T G T T T T T C C T A A A A
C A G G G G G A A T T G G T A C A A T T G T C T A T A T A T A T A G T T G G T T C T A C T T T T A T G A T A C T T A C C A T T T G T T C T
T T C C G T C G T A A A C A A T T G

SEQ ID NO. 19

45 M K K R Q K I W R G L S V T L L I L S Q I P F G I L V Q E T Q D T N Q A L G K V I V K K T G D N A T P L G K A T F V L K N D N D K S E
T S H E T V E G S G E A T F E N I K P G D Y T L R E E T A P I G Y K K T D K T W K V K V A D N G A T I I E G M D A D K A E K R K E V L N
A Q Y P K S A I Y E D T K E N Y P L V N V E G S K V G E Q Y K A L N P I N G K D G R R E I A E G W L S K K I T G V N D L D K N Y K I E
L T V E G K T T V E T K E L N Q P L D V V L L D N S N S M N N E R A N N S Q R A L K A G E A V E K L I D K I T S N K D N R V A L V T Y
A S T I F D G T E A T V S K G V A D Q N G K A L N D S V S W D Y H K T T F T A T T H N Y S Y L N L T N D A N E V N I L K S R I P K E A E
50 H I N G D R T L Y Q F G A T F T Q K A L M K A N E I L E T Q S S N A R K K L I F H V T D G V P T M S Y A I N F N P Y I S T S Y Q N Q F N
S F L N K I P D R S G I L Q E D F I I N G D D Y Q I V K G D G E S F K L F S D R K V P V T G G T T Q A A Y R V P Q N Q L S V M S N E G Y
A I N S G Y I Y L Y W R D Y N W V Y P F D P K T K K V S A T K Q I K T H G E P T T L Y F N G N I R P K G Y D I F T V G I G V N G D P G A
T P L E A E K F M Q S I S S K T E N Y T N V D D T N K I Y D E L N K Y F K T I V E E K H S I V D G N V T D P M G E M I E F Q L K N G Q S

FTHDDYVLVGNDGSQKNGVALGGPNSDGGILKDVTVTYDKTSQTIKINHLNLGSGQKVVLTYDVRLLK
 DNYISNKFYNTNNRRTTSLPKSEKEPNTIRDFPIPKIRDVREFFVLTISNQKKMGEVEFIKVNKDKHSE
 SLLGAKFQLQIEKDFSGYKQFVPEGSDVTTKNDGKIYFKALQDGNKLYEISSPDGYIEVKTTPVVTFT
 TIQNGEVTNLKADPNANKNQIGYLEGNGKHLITNTPKRPPGVFPKTGGIGTIVYILVGSTFMILTICS
 5 FRRKQL

GBS 104 contains an N-terminal leader or signal sequence region which is indicated by the
 underlined sequence at the beginning of SEQ ID NO 19 above. In one embodiment, one or more
 amino acid sequences from the leader or signal sequence region of GBS 104 are removed. An
 10 example of such a GBS 104 fragment is set forth below as SEQ ID NO 20.

SEQ ID NO 20

GETQDTNQALGKVIVKKTGDNATPLGKATFVLKNDNDKSETSHETVEGSGEATFENIKPGDYTLREET
 APIGYKKTDKTWKVKVADNGATIIEGMDADKAEKRKEVLNAQYPSAIYEDTKENYPLVNVEGSKVGE
 15 QYKALNPINGKDGRRREIAEGWLSKKITGVNDLDKNKYKIELTVEGKTTVETKELNQPLDVVLLDNSN
 SMNNERANNSQRALKAGEAVEKLIDKITSNKDNRVALVTYASTIFDGTEATVSKGVADQNGKALNDSV
 SWDYHKTTFTATTHNYSYLNLTNDANEVNILKSRIPEAEHINGDRTLYQFGATFTQKALMKANEILE
 TQSSNARKKLI FHVTDGVPTMSYAINFNPIYSTSYQNQFNSFLNKIPDRSGILQEDFIINGDDYQIVK
 20 GDGESFKLFSDRKVPVTGGTTQAAYRVPQNQLSVMSNEGYAINSGYIYLYWRDYNWVYPFDPKTKKVS
 ATKQIKTHGEPTTLYFNGNIRPKGYDIFTVGIGVNGDPGATPLEAEKFMQSISSKTENYTNVDDTNKI
 YDELNKYFKTIVEEKHSIVDGNVTDPMGEMIEFQLKNGQSFTHDDYVLVGNDGSQKNGVALGGPNSD
 GGILKDVTVTYDKTSQTIKINHLNLGSGQKVVLTYDVRLLKNDYISNKFYNTNNRRTTSLPKSEKEPNTI
 25 RDFPIPKIRDVREFFVLTISNQKKMGEVEFIKVNKDKHSESLGAKFQLQIEKDFSGYKQFVPEGSDV
 TTKNDGKIYFKALQDGNKLYEISSPDGYIEVKTTPVVTFTTIQNGEVTNLKADPNANKNQIGYLEGNG
 KHLITNTPKRPPGVFPKTGGIGTIVYILVGSTFMILTICSFRRKQL

GBS 104 contains a C-terminal transmembrane and/or cytoplasmic region which is indicated
 by the underlined region near the end of SEQ ID NO 19 above. In one embodiment, one or more
 amino acids from the transmembrane or cytoplasmic regions are removed. An example of such a
 30 GBS 104 fragment is set forth below as SEQ ID NO 21.

SEQ ID NO: 21

MKKRQKIWRGLSVTLILLSQIPFGILVQGETQDTNQALGKVIVKKTGDNATPLGKATFVLKNDNDKSE
 TSHETVEGSGEATFENIKPGDYTLREETAPIGYKKTDKTWKVKVADNGATIIEGMDADKAEKRKEVLN
 35 AQYPSAIYEDTKENYPLVNVEGSKVGEQYKALNPINGKDGRRREIAEGWLSKKITGVNDLDKNKYKIE
 LTVEGKTTVETKELNQPLDVVLLDNSNSMNNERANNSQRALKAGEAVEKLIDKITSNKDNRVALVTY
 ASTIFDGTEATVSKGVADQNGKALNDSVSWDYHKTTFTATTHNYSYLNLTNDANEVNILKSRIPEAE
 HINGDRTLYQFGATFTQKALMKANEILETQSSNARKKLI FHVTDGVPTMSYAINFNPIYSTSYQNQFN
 40 SFLNKIPDRSGILQEDFIINGDDYQIVKGDGESFKLFSDRKVPVTGGTTQAAYRVPQNQLSVMSNEGY
 AINSGYIYLYWRDYNWVYPFDPKTKKVSATKQIKTHGEPTTLYFNGNIRPKGYDIFTVGIGVNGDPA
 TPLEAEKFMQSISSKTENYTNVDDTNKIYDELNKYFKTIVEEKHSIVDGNVTDPMGEMIEFQLKNGQS
 FTHDDYVLVGNDGSQKNGVALGGPNSDGGILKDVTVTYDKTSQTIKINHLNLGSGQKVVLTYDVRLLK
 DNYISNKFYNTNNRRTTSLPKSEKEPNTIRDFPIPKIRDVREFFVLTISNQKKMGEVEFIKVNKDKHSE
 45 SLLGAKFQLQIEKDFSGYKQFVPEGSDVTTKNDGKIYFKALQDGNKLYEISSPDGYIEVKTTPVVTFT
 TIQNGEVTNLKADPNANKNQIGYLEGNGKHLITNT

In one embodiment, one or more amino acids from the leader or signal sequence region and one or more amino acids from the transmembrane or cytoplasmic regions are removed. An example of such a GBS 104 fragment is set forth below as SEQ ID NO 22.

5 **SEQ ID NO: 22**

GETQDTNQALGKVIIVKKTGDNATPLGKATFVLKNDNDKSETSHETVEGSGEATFENIKPGDYTLREET
APIGYKKTDKTWKVKVADNGATIIIEGMDADKAERKEVLNAQYPKSAIYEDTKENYPLVNVEGSKVGE
QYKALNPINGKDGRRERIEAGWLSKKITGVNDLDKNKYKIELTVEGKTTVETKELNQPLDVVLLDNSN
10 SMNNERANNSQRALKAGEAVEKLIDKITSNKDNRVALVTYASTIFDGTEATVSKGVADQNGKALNDSV
SWDYHKTTFTATTHNYSYLNLTNDANEVNILKSRIPEAEHINGDRTLYQFGATFTQKALMKANEILE
TQSSNARKKLI FHVTDGVPMTSYAINFNPIYSTSYQNQFNSFLNKIPDRSGILQEDFIINGDDYQIVK
GDGESFKLFSDRKVPVTGGTTQAAYRVPQNQLSVMSNEGYAINSGYIYLYWRDYNWVYPFDPKTKKVS
ATKQIKTHGEPTTLYFNGNIRPKGYDIFTVGIGVNGDPGATPLEAEKFMQSISSKTENYTNVDDTNKI
YDELNKYFKTIVEEKHSIVDGNVTDPMGEMIEFQLKNGQSFTHDDYVLVGNDSQLKNGVALGGPNSD
15 GGILKDVTVTYDKTSQTIKINHLNLGSGQKVLTVDVRLKDNYSNKFYNTNNRTTSLSPKSEKEPNTI
RDFPIPKIRDVREFPVLTI SNQKKMGEVEFIKVNKDKHSESLLGAKFQLQIEKDFSGYKQFVPEGSDV
TTKNDGKIYFKALQDGNKYLYEISSPDGYIEVKTKPVVFTI QNGEVTNLKADPNANKNQIGYLEGNG
KHLITNT

20 In other embodiments, additional fragments of GBS 104 are provided including an 830 amino acid fragment of GBS 104 of amino acids 28-858, a 359 amino acid fragment of GBS 104 of amino acids 28-387, a 581 amino acid fragment of GBS 104 of amino acids 28-609, or a 740 amino acid fragment of GBS 104 of amino acids 28-768.

25 GBS 184

GBS 184 refers to a putative lipoprotein. Nucleotide and amino acid sequences of GBS 184 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 1977 and SEQ ID 1978. These sequences are also set forth below as SEQ ID NOS 23 and 24.

30 **SEQ ID NO: 23**

ATGAAAAAACAAAACTATTACTGCTTATTGGAGGCTTATTAATAATGATAATGATGACAGCATGTAA
GGATTCAAAAATCCCAGAAAACCGCACAAAGGAAGAGTACCAAGCTGAACAAAATTTTAAACCGTTTT
TTGAGTTTTTTAGCACAAAAAGATAAAGATTTGAGCAAAATACAAAAATACTTACTATTAGTATCGGAT
TCAGGTGATGCATTAGATTTAGAATATTTCTATAGTATTCAAGATTTAAAAAAAATAAGGATTTAGG
35 GAAGTTTGAAACAAGAAAAAGTCAAATAGAAAAGCCGGGTGGCTATAATGAGTTAGAAAATAAGAGG
TCCCATTTGAATATTTTAAAAATAATATAGTTTATCCAAAAGGAAAACCGAATATTACATTTGATGAC
TTTATTATCGGAGCAATGGATACTAAAGAATTAAAAGAATTAAAAAAATTAAAAGTAAAAAGTTATTT
ATTAAACATCCGGAAGTGAAGATATAACATATGAATTGCCGACACAGTCGAAGCTTATTA
AAAA

40

SEQ ID NO: 24

MKKQKLLLLIGLLIMIMMTACKDSKIPENRTKEEYQAEQNFKPFFFEFLAQKDKDLSKIQKYLLLVSD
SGDALDLEYFYSIQDLKKNKDLGKFETRKSQIEKPGGYNELENKEVPFEYFKNIVYPKGKPNITFDD
FIIGAMDTKELKELKKLKVKS YLLKHPETELKDI TYELPTQSKLIKK

45

GBS 184 contains a N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO 24, above. In one embodiment, one or more amino acids from the leader or signal sequence are removed from GBS 184. An example of such a GBS 184 fragment is set forth below as SEQ ID NO: 25.

SEQ ID NO: 25

KDSKIPENRTKEEYQAEQNFKPFEEFLAQKDKDLSKIQKYLLLVSDSGDALDLEYFYYSIQDLKKNKDL
GKFETRKSQIEKPGGYNELENKEVPFEYFKNNIVYPKGKPNITFDDFIIGAMDTKELKELKKLKVKS
YLLKHPETELKDITYELPTQSKLIKK

GBS 276

GBS 276 refers to a C5a peptidase. Nucleotide and amino acid sequences of GBS 276 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 8941 and SEQ ID 8942. These sequences are set forth below as SEQ ID NOS 26 and 27:

SEQ ID NO. 26

TTGCGTAAAAACAAAACTACCATTTGATAAACTTGCCATTGCGCTTATATCTACGAGCATCTTGCT
CAATGCACAATCAGACATTAAAGCAAATACTGTGACAGAAGACACTCCTGCTACCGAACAAGCCGTAG
AACC CCCACAACCAATAGCAGTTTCTGAGGAATCACGATCATCAAAGGAACTAAAACCTCACAACT
CCTAGTGATGTAGGAGAAACAGTAGCAGATGACGTAATGATCTAGCCCCCTCAAGCTCCTGCTAAAAC
TGCTGATACACCAGCAACCTCAAAGCGACTATTAGGGATTGTAACGACCCTTCTCATGTCAAACCC
TGCAAGGAAAAAGCAGGCAAGGGAGCTGGGACCGTTGTTGCAGTGATTGATGCTGGTTTTGATAAAAT
CATGAAGCGTGGCGCTTAACAGACAAAACCTAAAGCACGTTACCAATCAAAGAAAATCTTGAAAAAGC
TAAAAAAGAGCACGGTATTACCTATGGCGAGTGGGTCAATGATAAGGTTGCTTATTACCACGACTATA
GTAAAGATGGTAAAAACGCTGTTGATCAAGAACACGGGCACACACGCTGTCAGGGATCTTGTCAGGAAAT
GCTCCATCTGAAATGAAAGAACCTTACCGCCTAGAAGGTGCGATGCCTGAGGCTCAATTGCTTTTGAT
GCGTGTCGAAATTGTAATGGACTAGCAGACTATGCTCGTAACTACGCTCAAGCTATCAGAGATGCTG
TCAACTTGGGAGCTAAGGTGATTAATATGAGCTTTGGTAATGCTGCACTAGCTTACGCCAACCTTCCA
GACGAAACCAAAAAAGCCTTTGACTATGCCAAATCAAAGGTGTTAGCATTGTGACCTCAGCTGGTAA
TGATAGTAGCTTTGGGGGCAAGCCCCGTCTACCTCTAGCAGATCATCCTGATTATGGGGTGGTTGGGA
CACCTGCAGCGGCAGATTCAACATTGACAGTTGCTTCTTACAGCCCAGATAAACAGCTCACTGAACT
GCTACGGTCAAAACAGACGATCATCAAGATAAAGAAATGCCTGTTATTTCAACAAACCGTTTTGAGCC
AAACAAGGCTTACGACTATGCTTATGCTAATCGTGGTACGAAAGAGGATGATTTTAAGGATGTCGAAG
GTAAGATTGCCCTTATTGAACGTGGCGATATTGATTTCAAAGATAAGATTGCAAACGCTAAAAAAGCT
GGTGCTGTAGGGGTCTTGATCTATGACAATCAAGACAAGGGCTTCCCGATTGAATTGCCAAATGTTGA
CCAGATGCCTGCGGCCCTTATCAGTCGAAGAGACGGTCTCTTATTAAAAGACAATCCCCCAAAACCA
TTACCTTCAATGCGACACCTAAGGTATTGCCAACAGCAAGTGGCACCAAACTAAGCCGCTTCTCAAGC
TGGGGTCTGACAGCTGACGGCAATATTAAACCGGATATTGCAGCACCCGGCCAAGATATTTTGTCTATC
AGTGGCTAACAACAAGTATGCCAACTTTCTGGAAGTAGTATGTCTGCACCATTGGTAGCGGGTATCA
TGGGACTGTTGCAAAAGCAATATGAGACACAGTATCCTGATATGACACCATCAGAGCGTCTTGATTTA
GCTAAGAAAGTATTGATGAGCTCAGCAACTGCCCTATATGATGAAGATGAAAAAGCTTATTTTTCTCC
TCGCCAACAGGGAGCAGGAGCAGTCGATGCTAAAAAAGCTTCAGCAGCAACGATGTATGTAACAGATA
AGGACAATACCTCAAGCAAGGTTACCTGAACAATGTTTCTGATAAATTTGAAGTAACAGTAACAGTT
CACAAACAATCTGATAAACCTCAAGAGTTGTATTACCAAGTAAGTTCAAACAGATAAAGTAGATGG
AAAACACTTTGCCTTGGCTCCTAAAGCATTTGTATGAGACATCATGGCAAAAAATCACAAATCCAGCCA
ATAGCAGCAAAACAGTCACCGTTCCAATCGATGCTAGTCGATTTAGCAAGGACTTGCTTGCCCAATG
AAAAATGGCTATTTCTTAGAAGGTTTTGTTTCGTTCAAACAAGATCCTACAAAAGAAGAGCTTATGAG
CATTCATATATTGGTTTTCCGAGGTGATTTTGGCAATCTGTCAGCCTTAGAAAAACCAATCTATGATA

GCAAAGACGGTAGCAGCTACTATCATGAAGCAAATAGTGATGCCAAAGACCAATTAGATGGTGATGGA
 TTACAGTTTTTACGCTCTGAAAAATAACTTTACAGCACTTACCACAGAGTCTAACCCATGGACGATTAT
 TAAAGCTGTCAAAGAAGGGGTTGAAAACATAGAGGATATCGAATCTTCAGAGATCACAGAAACCATT
 TTGCAGGTACTTTTGCAAACAAGACGATGATAGCCACTACTATATCCACCGTCACGCTAATGGCAAA
 5 CCATATGCTGCGATCTCTCCAAATGGGGACGGTAACAGAGATTATGTCCAATTCGAAGGTACTTTCTT
 GCGTAATGCTAAAAACCTTGTGGCTGAAGTCTTGGACAAAGAAGGAAATGTTGTTTGGACAAGTGAGG
 TAACCGAGCAAGTTGTTAAAACTACAACAATGACTTGGCAAGCACACTTGGTTCAACCCGTTTGA
 AAAACGCGTTGGGACGGTAAAGATAAAGACGGCAAAGTTGTTGCTAACGGAACCTACACCTATCGTGT
 TCGCTACACGCCGATTAGCTCAGGTGCAAAAGAACAACACACTGATTTTGTGATGTGATTGACACAATA
 10 CGACACCTGAAGTCGCAACATCGGCAACATTCTCAACAGAAGATAGTCGTTTGACACTTGCATCTAAA
 CCAAAAACCAGCCAACCGGTTTACCGTGAGCGTATTGCTTACACTTATATGGATGAGGATCTGCCAAC
 AACAGAGTATATTTCTCCAAATGAAGATGGTACCTTTACTCTTCTGAAGAGGCTGAAACAATGGAAG
 GCGCTACTGTTCCATTGAAAATGTCAGACTTTACTTATGTTGTTGAAGATATGGCTGGTAACATCACT
 TATACACCAGTGACTAAGCTATTGGAGGGCCACTCTAATAAGCCAGAACAAGACGGTTCAGATCAAGC
 15 ACCAGACAAGAAACCAGAAGCTAAACCAGAACAAGACGGTTCAGGTCAAACACCAGATAAAAAAAG
 AACTAAACCAGAAAAAGATAGTTTCAAGTCAAACACCAGGTAAACTCCTCAAAAAGGTCAATCTTCT
 CGTACTCTAGAGAAACGATCTTCTAAGCGTGCTTTAGCTACAAAAGCATCAACAAGAGATCAGTTACC
 AACGACTAATGACAAGGATACAAATCGTTTACATCTCCTTAAGTTAGTTATGACCACTTTCTTCTTGG
 GA

SEQ ID NO. 27

MRKKQKLPEFDKLALISTSIILLNAQSDIKANTVTEDTPATEQAVEPPQPIAVSEESRSSKETKTSQT
 PSDVGETVADDANDLAPQAPAKTADTPATSKATIRDLNDPSHVKTLOEKAGKGAGTVVAVIDAGFDKN
 HEAWRLTDKTKARYQSKENLEKAKKEHGITYGEWVNDKVAYYHDYSKDGKNAVDQEHGTHVSGILSGN
 25 APSEMKEPYRLEGAMPEAQLLLMRVEIVNGLADYARNYAQAIRDAVNLGAKVINMSFGNAALAYANLP
 DETKKAFFDYAKSKGVSIVTSAGNDSSFSGKPRPLADHPDYGTVVGTAAADSTLTVASYSPOKQLTET
 ATVKTDHHDQKEMPVISTNRFEPNKAYDYAYANRGTKEDDFKDVGEKIALIERGIDIFDKKIANAKKA
 GAVGVLIYDNQDKGFPIELPNVDQMPAAFISSRDGLLLKDNPPKTIITFNATPKVLPTASGKLSRFSS
 WGLTADGNIKPDIAAPGQDILSSVANNKYAKLSGTSMSAPLVAGIMGLLQKQYETQYPMPTPSERLDL
 30 AKKVLMS SATALYDEDEKAYFS PRQGGAGAVDAKKASAATMYVTDKNTSSKVHLNNVSDKFEVTVTV
 HNKSDKPQELYQVTVQTDKVDGKHFALAPKALYETSWQKITIPANSSKQVTVPIDASRFSKDLLAQM
 KNGYFLEGGFVRFKQDPTKEELMSIPYIGFRGDFGNLSALEKPIYDSKDGSSYYHEANSDAKDQLDGDG
 LQFYALKNNFTALTTESNPWTIIKAVKEGVENIEDIESSEITETIFAGTFAKQDDDSHYIHRHANGK
 PYAAISPNGDGNRDYVQFQGTFLRNAKNLVAEVL DKEGNVVTSEVTEQVVKNYNNDLASTLGSTRFE
 35 KTRWDGKDKDGKVVANGTYTYRVRYTPISSGAKEQHTDFDVIVDNTTPEVATSATFSTEDSRLTLASK
 PKTSQPVYRERIAITYMDEDLPTTEYISPNEGDGFTLPEEAETMEGATVPLKMSDFTYVVEDMAGNIT
 YTPVTKLLEGHSENKPEQDGS DQAPDKKPEAKPEQDGS GQTPDKKKETKPEKDSSGQTPGKTPQKGQSS
 RTLEKRS SKRALATKASTRDQLPTTNDKDTNRLHLLKLVMTTFFLG

40 GBS 276 contains an N-terminal leader or signal sequence region which is indicated by the
 underlined sequence at the beginning of SEQ ID NO: 27 above. In one embodiment, one or more
 amino acids from the leader or signal sequence region of GBS 276 are removed. An example of such
 a GBS 276 fragment is set forth below as SEQ ID NO: 28.

SEQ ID NO: 28

QSDIKANTVTEDTPATEQAVEPPQPIAVSEESRSSKETKTSQTPSDVGETVADDANDLAPQAPAKTAD
 TPATSKATIRDLNDPSHVKTLQEKAGKGAGTVVAVIDAGFDKNHEAWRLTDKTKARYQSKENLEKAKK
 5 EHGITYGEWVNDKVAYYHDYSKDGNNAVDQEHGTHVSGILSGNAPSEMKEPYRLEGAMPEAQLLLLMRV
 EIVNGLADYARNYAQAIRDAVN LGAKVINMSFGNAALAYANLPDETKKAFDYAKSKGVSIVTSAGNDS
 SFGGKPRPLADHPDYGVVGT PAAADSTLTVASYS PDKQLTETATVKTDHHDQDKEMPVISTNRFEPNK
 AYDYAYANRGTKEDDFKDVEGKIALIERGDI DFKD KIANAKKAGAVGVLIYDNQDKGFPIELPNVDQM
 PAAFI SRRDGLLLKDNPPKTITFNATPKVLPTASGTKLSRFSSWGLTADGNIKPDIAAPGQDILSSVA
 10 NNKYAKLSGT SMSAPLVAGIMGLLQKQYETQYPDMTPSERLDLAKKVLMS SATALYDEDEKAYFS PRQ
 QGAGAVDAKKASAATMYVTDKNTSSKVHLNNVSDKFEVTVTVHNKSDKPKQELYQVTVQTDKVDGKH
 FALAPKALYETSWQKITIPANSSKQVTVPIDASRFSKDLLAQMKNGYFLEGFVRFKQDPTKEELMSIP
 YIGFRGDFGNLSALEKPIYDSKDGS SYHEANS DAKDQLDGDGLQFYALKNNFTALTTESNPWTIIKA
 VKEGVENIEDIESSEITETIFAGTFAKQDDDSHYIHRHANGKPYAAISPNGDGNRDYVQFGTFLRN
 15 AKNLVAEVL DKEGNVVTSEVTEQVVKNNNDLASTLGSTRFEKTRWDGKDKDGKVVANGTYTYRVRY
 TPISSGAKEQHTDFDVI DVNTTPEVATSATFSTEDSRLTLASKPKTSQPVYRERIAAYTYMDEDLPTTE
 YISPNE DGTFTLPEEAETMEGATVPLKMSDFTYVVEDMAGNITYTPVTKLLEGH SNKPEQDGS DQAPD
 KKPEAKPEQDGS GQTPDKKKETKPEKDSSGQTPGKTPQKGQSSRTLEKRSSKRALATKASTRDQLPTT
 NDKDTNRLHLLKLVMTTFFLG

GBS 276 contains a C-terminal transmembrane and/or cytoplasmic region which is indicated
 by the underlined sequence near the end of SEQ ID NO: 27 above. In one embodiment, one or more
 amino acids from the transmembrane or cytoplasmic regions of GBS 276 are removed. An example
 of such a GBS 276 fragment is set forth below as SEQ ID NO: 29.

SEQ ID NO: 29

MRKKQKLPFDKLAIALISTSI LLNAQSDIKANTVTEDTPATEQAVEPPQPIAVSEESRSSKETKTSQTP
 PSDVGETVADDANDLAPQAPAKTADTPATSKATIRDLNDPSHVKTLQEKAGKGAGTVVAVIDAGFDKN
 HEAWRLTDKTKARYQSKENLEKAKKEHGITYGEWVNDKVAYYHDYSKDGNNAVDQEHGTHVSGILSGN
 30 APSEMKEPYRLEGAMPEAQLLLLMRVEIVNGLADYARNYAQAIRDAVN LGAKVINMSFGNAALAYANLP
 DETKKA FDYAKSKGVSIVTSAGNDS SFGGKPRPLADHPDYGVVGT PAAADSTLTVASYS PDKQLTET
 ATVKTDDHHDQDKEMPVISTNRFEPNKAYDYAYANRGTKEDDFKDVEGKIALIERGDI DFKD KIANAKKA
 GAVGVLIYDNQDKGFPIELPNVDQM PAAFI SRRDGLLLKDNPPKTITFNATPKVLPTASGTKLSRFSS
 WGLTADGNIKPDIAAPGQDILSSVANNKYAKLSGT SMSAPLVAGIMGLLQKQYETQYPDMTPSERLDL
 35 AKKVLMS SATALYDEDEKAYFS PRQQGAGAVDAKKASAATMYVTDKNTSSKVHLNNVSDKFEVTVTV
 HNKSDKPKQELYQVTVQTDKVDGKH FALAPKALYETSWQKITIPANSSKQVTVPIDASRFSKDLLAQM
 KNGYFLEGFVRFKQDPTKEELMSIPYIGFRGDFGNLSALEKPIYDSKDGS SYHEANS DAKDQLDGDG
 LQFYALKNNFTALTTESNPWTIIKAVKEGVENIEDIESSEITETIFAGTFAKQDDDSHYIHRHANGK
 PYAAISPNGDGNRDYVQFGTFLRNAKNLVAEVL DKEGNVVTSEVTEQVVKNNNDLASTLGSTRFE
 40 KTRWDGKDKDGKVVANGTYTYRVRYTPISSGAKEQHTDFDVI DVNTTPEVATSATFSTEDSRLTLASK
 PKTSQPVYRERIAAYTYMDEDLPTTEYISPNE DGTFTLPEEAETMEGATVPLKMSDFTYVVEDMAGNIT
 YTPVTKLLEGH SNKPEQDGS DQAPDKKPEAKPEQDGS GQTPDKKKETKPEKDSSGQTPGKTPQKGQSS
 RTLEKRSSKRALATK

In one embodiment, one or more amino acids from the leader or signal sequence region and
 one or more amino acids from the transmembrane or cytoplasmic regions of GBS 276 are removed.
 An example of such a GBS 276 fragment is set forth below as SEQ ID NO: 30.

SEQ ID NO: 30

QSDIKANTVTEDTPEQAVEPPQPIAVSEESRSSKETKTSQTPSDVGETVADDANDLAPQAPAKTAD
 TPATS KATIRDLNDPSHVKTLEKAGKGAGTVVAVIDAGFDKNHEAWRLTDKTKARYQSKENLEKAKK
 EHGITYGEWVNDKVAYYHDYSKDGKNAVDQEHGTHVSGILSGNAPSEMKEPYRLEGAMPEAQLLLMRV
 EIVNGLADYARNYAQAIRDAVN LGAKVINMSFGNAALAYANLPDETKKAFDYAKSKGVSIVTSAGNDS
 5 SFGGKPRPLADHPDYGVVGT PAAADSTLTVASYS PDKQLTETATVKTDHDDHDKEMPVISTNRFE PNK
 AYDYAYANRGTKEDDFKDVEGKIALIERGDI DFKD KIANAKKAGAVGVLIYDNQDKGFPIELPNVDQM
 PAAFI SRRDGLLLKDNPPKTITFNATPKVLPTASGTKLSRFSSWGLTADGNIKPDIAAPGQDILSSVA
 NNKYAKLSGTSMSAPLVAGIMGLLQKQYETQYPDMTPSERLDLAKKVLMS SATALYDEDEKAYFS PRQ
 10 QGAGAVDAKKASAATMYVTDKNTSSKVHLNNVSDKFEVTVTVHNKSDKPQELYQVTVQTDKVDGKH
 FALAPKALYETSWQKITIPANSSKQVTVPIDASRFSKDLLAQMKNGYFLEGEFVRFKQDPTKEELMSIP
 YIGFRGDFGNLSALEKPIYDSKDGSSYYHEANS DAKDQLDGDGLQFYALKNNFTALTTESNPWTI IKA
 VKEGVENIEDIESSEITETIFAGTFAKQDDDSHYIHRHANGKPYAAISPNGDGNRDYVQFQGTFLRN
 AKNLVAEVL DKEGNVVTSEVTEQVVKNNNDLASTLGSTRFEKTRWDGKDKDGKVVANGTYTYRVRY
 15 TPISSGAKEQHTDFDVIDNTTPEVATSATFSTEDSRLTLASKPKTSQPVYRERIAITYMDEDLPTTE
 YISPNE DGTFTLP EEAETMEGATVPLKMSDFTYVVEDMAGNITYTPVTKLLEGH SNKPEQDGS DQAPD
 KKPEAKPEQDGS GQTPDKKKETKPEKDSSGQTPGKTPQKGQSSRTLEKRSSKRALATK

Further description of GBS 276 can be found in the following references: Qi Chen et al.,
 “Immunization with C5a Peptidase or Peptidase-Type III Polysaccharide conjugate Vaccines
 20 Enhances Clearance of Group B Streptococci from Lungs of Infected Mice”, *Infection and Immunity*
 (2002) 70 (11):6409 – 6415; Beckmann et al., “Identification of Novel Adhesions from Group B
 Streptococci by Use of Phage Display Reveals that C5a Peptidase Mediates Fibronectin Binding”
Infection and Immunity (2002) 70(6):2869 – 2876; Cheng et al., “The Group B Streptococcal C5a
 Peptidase Is Both a Specific Protease and an Invasin” *Infection and Immunity* (2002) 70(5) 2408 –
 25 2413; and Cheng et al., “Antibody against Surface-Bound C5a Peptidase Is Opsonic and Initiates
 Macrophage Killing of Group B Streptococci” *Infection and Immunity* (2001) 69(4):2302 – 2308.

GBS 305

GBS 305 refers to a UDP-N-acetylmuramoylalanine--D-glutamate ligase, also referred to
 30 as Mur D. Nucleotide and amino acid sequences of GBS 305 sequenced from serotype V isolated
 strain 2603 V/R are set forth in Ref. 2 as SEQ ID 207 and SEQ ID 208. These sequences are set forth
 below as SEQ ID NOS 31 and 32:

SEQ ID NO. 31

35 ATGGGACGAGTAATGAAAACAATAACAACATTTGAAAATAAAAAAGTTTTAGTCCTTGGTTTAGCACG
 ATCTGGAGAAGCTGCTGCACGTTTGTTAGCTAAGTTAGGAGCAATAGTGACAGTTAATGATGGCAAAC
 CATTTGATGAAAATCCAACAGCACAGTCTTTGTTGGAAGAGGGTATTAAAGTGGTTTGTGGTAGTCAT
 CCTTTAGAATTGTTAGATGAGGATTTTTGTTACATGATTAAAAATCCAGGAATACCTTATAACAATCC
 TATGGTCAAAAAAGCATTAGAAAAACAATCCCTGTTTTGACTGAAGTGGAATTAGCATACTTAGTTT
 40 CAGAATCTCAGCTAATAGGTATTACAGGCTCTAACGGGAAAACGACAACGACAACGATGATTGCAGAA
 GTCTTAAATGCTGGAGGTCAGAGAGGTTTGTTAGCTGGGAATATCGGCTTTCCTGCTAGTGAAGTTGT
 TCAGGCTGCGAATGATAAAGATACTCTAGTTATGGAATTATCAAGTTTTTCAGCTAATGGGAGTTAAGG
 AATTTGTCCTCATATTGCAGTAATTACTAATTTAATGCCAACTCATTTAGATTATCATGGGTCCTTTT
 45 GAAGATTATGTTGCTGCAAAATGGAATATCCAAAATCAAATGTCTTCATCTGATTTTTTTGGTACTTAA
 TTTTAATCAAGGTATTTCTAAAGAGTTAGCTAAAATACTAAAGCAACAATCGTTCCTTTCTCTACTA
 CGGAAAAAGTTGATGGTGCTTACGTACAAGACAAGCAACTTTTCTATAAAGGGGAGAATATTATGTCA

GTAGATGACATTGGTGTCCAGGAAGCCATAACGTAGAGAATGCTCTAGCAACTATTGCGGTTGCTAA
 ACTGGCTGGTATCAGTAATCAAGTTATTAGAGAACTTTAAGCAATTTTGGAGGTGTTAAACACCGCT
 TGCAATCACTCGGTAAGGTTTCATGGTATTAGTTTCTATAACGACAGCAAGTCAACTAATATATTGGCA
 ACTCAAAAAGCATTATCTGGCTTTGATAATACTAAAGTTATCCTAATTGCAGGAGGTCTTGATCGCGG
 5 TAATGAGTTTGTGAATTGATACCAGATATCACTGGACTTAAACATATGGTTGTTTTAGGGGAATCGG
 CATCTCGAGTAAAACGTGCTGCACAAAAAGCAGGAGTAACCTTATAGCGATGCTTTAGATGTTAGAGAT
 GCGGTACATAAAGCTTATGAGGTGGCACAACAGGGCGATGTTATCTTGCTAAGTCCTGCAAATGCATC
 ATGGGACATGTATAAGAATTTCAAGTCCGTGGTGATGAATTCATTGATACTTTTCGAAAGTCTTAGAG
 GAGAG

SEQ ID NO. 32

MGRVMKTITTTFENKKVLVLGLARSGEAAARLLAKLGAIIVTVNDGKPFDENPTAQSLLEEGIKVVCGSH
 PLELLDEDFCYMIKNPGIPYNNPMVKKALEKQIPVLTEVELAYLVSESQIGITGSNGKTTTTTMI
 VLNAGGQRGLLAGNIGFPASEVVQAANDKDTLVMELSSFQLMGVKEFRPHIAVITNLMPTHLDYHGSF
 15 EDYVAAKWNINQNMSSSDFLVNLFNQGISKEKAKTTKATIVPFSTTEKVDGAYVQDKQLFYKGENIMS
 VDDIGVPGSHNVENALATIIVAKLAGISNQVIRETSLNFGGVKHLQSLGKVHGISFYNSKSTNILA
TQKALSGFDNTKVILIAAGGLDRGNEFDELIPDITGLKHMVVLGESASRVKRAAQKAGVTYSDALDVRD
AVHKAYEVAQQGDVILLSPANASWDMYKNFEVRGDEFIDTFESLRGE

20 GBS 305 contains an N-terminal leader or signal sequence region which is indicated by the
 underlined sequence at the beginning of SEQ ID NO: 32 above. In one embodiment, one or more
 amino acids from the leader or signal sequence region are removed from GBS 305. An example of
 such a GBS 305 fragment is set forth below as SEQ ID NO: 33.

SEQ ID NO: 33

ITTFENKKVLVLGLARSGEAAARLLAKLGAIIVTVNDGKPFDENPTAQSLLEEGIKVVCGSHPLELLDE
 DFCYMIKNPGIPYNNPMVKKALEKQIPVLTEVELAYLVSESQIGITGSNGKTTTTTMI
 RGLLAGNIGFPASEVVQAANDKDTLVMELSSFQLMGVKEFRPHIAVITNLMPTHLDYHGSFEDYVAAK
 25 WNIQNQNMSSSDFLVNLFNQGISKEKAKTTKATIVPFSTTEKVDGAYVQDKQLFYKGENIMSVDDIGV
 30 GSHNVENALATIIVAKLAGISNQVIRETSLNFGGVKHLQSLGKVHGISFYNSKSTNILATQKALSG
 FDNTKVILIAAGGLDRGNEFDELIPDITGLKHMVVLGESASRVKRAAQKAGVTYSDALDVRDAVHKAYE
 VAQQGDVILLSPANASWDMYKNFEVRGDEFIDTFESLRGE

35 GBS 305 contains a C-terminal transmembrane or cytoplasmic region indicated by the
 underlined sequence near the end of SEQ ID NO: 32 above. In one embodiment, one or more amino
 acids from the transmembrane or cytoplasmic regions are removed from GBS 305. An example of
 such a GBS 305 fragment is set forth below as SEQ ID NO: 34.

SEQ ID NO: 34

40 MGRVMKTITTTFENKKVLVLGLARSGEAAARLLAKLGAIIVTVNDGKPFDENPTAQSLLEEGIKVVCGSH
 PLELLDEDFCYMIKNPGIPYNNPMVKKALEKQIPVLTEVELAYLVSESQIGITGSNGKTTTTTMI
 VLNAGGQRGLLAGNIGFPASEVVQAANDKDTLVMELSSFQLMGVKEFRPHIAVITNLMPTHLDYHGSF
 EDYVAAKWNINQNMSSSDFLVNLFNQGISKEKAKTTKATIVPFSTTEKVDGAYVQDKQLFYKGENIMS
 45 VDDIGVPGSHNVENALATIIVAKLAGISNQVIRETSLNFGGVKHLQSLGKVHGISFYNSK

In one embodiment one or more amino acids from the leader or signal sequence region and one or more amino acids from the transmembrane or cytoplasmic regions are removed from GBS 305. An example of such a GBS 305 fragment is set forth below as SEQ ID NO: 35.

5 SEQ ID NO: 35

ITTFENKKVLVLGLARSGEAAARLLAKLGAIIVTVNDGKPFDENPTAQSLLEEGIKVVCGSHPLELLDE
DFCYMIKNPGIPYNNPMVKKALEKQIPVLTEVELAYLVSESQILIGITGSNGKTTTTTMMIAEVLNAGGQ
RGLLAGNIGFPASEVVQAANDKDTLVMELSSFQLMGVKEFRPHIAVITNLMPTHLDYHGSFEDYVAAK
10 WNIQNQMSSSDFLVLNFNQGISKEKLAKTTKATIVPFSTTEKVDGAYVQDKQLFYKGENIMSVDDIGVP
GSHNVENALATIATAVAKLAGISNQVIRETLSNFGGVKHRLQSLGKVHGISFYNSDK

GBS 322

GBS 322 refers to a surface immunogenic protein, also referred to as “sip”. Nucleotide and amino acid sequences of GBS 322 sequenced from serotype V isolated strain 2603 V/R are set forth in
15 Ref. 2 as SEQ ID 8539 and SEQ ID 8540. These sequences are set forth below as SEQ ID NOS 36
and 37:

SEQ ID NO. 36

ATGAATAAAAAGGTACTATTGACATCGACAATGGCAGCTTCGCTATTATCAGTCGCAAGTGTTCAAGC
20 ACAAGAAACAGATACGACGTGGACAGCAGCTACTGTTTCAGAGGTAAAGGCTGATTTGGTAAAGCAAG
ACAAATAATCATCATATACTGTGAAATATGGTGATACCTAAGCGTTATTTTCAAGCAATGTCAATT
GATATGAATGTCTTAGCAAAAATAAATAACATTGCAGATATCAATCTTATTTATCCTGAGACAACACT
GACAGTAACTTACGATCAGAAGAGTCATACTGCCACTTCAATGAAAATAGAAACACCAGCAACAAATG
CTGCTGGTCAAACAACAGCTACTGTGGATTGAAAACCAATCAAGTTTCTGTTGCAGACCAAAAAGTT
25 TCTCTCAATACAATTTTCGGAAGGTATGACACCAGAAGCAGCAACAACGATTGTTTCGCCAATGAAGAC
ATATTCCTTCTGCGCCAGCTTTGAAATCAAAAGAAGTATTAGCACAAAGAGCAAGCTGTTAGTCAAGCAG
CAGCTAATGAACAGGTATCACCAGCTCCTGTGAAGTCGATTACTTCAGAAGTTCAGCAGCTAAAGAG
GAAGTTAAACCAACTCAGACGTCAGTCAGTCAGTCAACAACAGTATCACCAGCTTCTGTTGCCGCTGA
AACACCAGCTCCAGTAGCTAAAGTAGCACCGGTAAGAAGTGTAGCAGCCCCCTAGAGTGGCAAGTGTTA
30 AAGTAGTCACTCCTAAAGTAGAACTGGTGCATCACCAGAGCATGTATCAGCTCCAGCAGTTCTCTGTG
ACTACGACTTCACCAGCTACAGACAGTAAGTTACAAGCGACTGAAGTTAAGAGCGTTCCGGTAGCACA
AAAAGCTCCAACAGCAACACCGGTAGCACAACCAGCTTCAACAACAAATGCAGTAGCTGCACATCCTG
AAAATGCAGGGCTCCAACCTCATGTTGCAGCTTATAAAGAAAAAGTAGCGTCAACTTATGGAGTTAAT
GAATTCAGTACATAACCGTGCAGGAGATCCAGGTGATCATGGTAAAGGTTTAGCAGTTGACTTTATTGT
35 AGGTACTAATCAAGCACTTGGTAATAAAGTTGCACAGTACTCTACACAAAATATGGCAGCAAATAACA
TTTCATATGTTATCTGGCAACAAAAGTTTACTCAAATACAAACAGTATTTATGGACCTGCTAATACT
TGGAATGCAATGCCAGATCGTGGTGGCGTTACTGCCAACCACTATGACCACGTTACAGTATCATTTAA
CAAAATAATATAAAAAAGGAAGCTATTTGGCTTCTTTTTTATATGCCTTGAATAGACTTTCAAGGTTCT
TATATAATTTTATTA

40

SEQ ID NO. 37

MNKKVLLTSTMAASLLSVASVQAQETDTTWTARTVSEVKADLVKQDNKSSYTVKYGDTLSVISEAMS
DMNVLAKINNIADINLIYPETTLTVTYDQKSHTATSMKIETPATNAAGQTTATVDLKTNQVSVADQKV
SLNTISEGMTPEAATTIVSPMKTYSSAPALKSKEVLAQEQAVSQAAANEQVSPAPVKSITSEVPAAKE
45 EVKPTQTSVSQSTTVSPASVAAETPAPVAKVAPVRTVAAPRVASVKVVT PKVETGASPEHVSAPAVPV
TTTSPATDSKLQATEVKSVPAQKAPTATPVAQPASTTNAVAHPENAGLQPHVAAYKEKVASTYGVN
EFSTYRAGDPGDHKGGLAVDFIVGTNQALGNKVAQYSTQNMAANNISYVIWQQKFYSNTNSIYGPANT
WNAMPDRGGVTANHYDHVHVSFNK

GBS 322 contains an N-terminal leader or signal sequence region which is indicated by the underlined sequence near the beginning of SEQ ID NO: 37. In one embodiment, one or more amino acids from the leader or signal sequence region of GBS 322 are removed. An example of such a GBS 322 fragment is set forth below as SEQ ID NO: 38.

SEQ ID NO: 38

DLVKQDNKSSYTVKYGDTLSVISEAMSIDMNVLAKINNIADINLIYPETTLTVTYDQKSHTATSMKIE
TPATNAAGQTTATVDLKTNQVSVADQKVSNTISEGMTPEAATTIVSPMKTYSSAPALKSKEVLAQEQ
AVSQAAANEQVSPAPVKSITSEVPAAKEEVKPTQTSVSVQSTTVSPASVAAETPAPVAKVAPVRTVAAP
RVASVKVVTPKVETGASPEHVSAPAVPVTSTPATDSKLQATEVKSVPVAQKAPTATPVAQPASTTNA
VAAHPENAGLQPHVAAYKEKVASTYGVNEFSTYRAGDPGDHKGGLAVDFIVGTNQALGNKVAQYSTQN
MAANNISYVIWQQKFYSNTNSIYGPANTWNPDRGGVTANHYDHHVHVSFNK

GBS 330

GBS 330 refers to a pyruvate kinase, also referred to as "pyk". Nucleotide and amino acid sequences of GBS 330 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 8791 and SEQ ID 8792. These sequences are set forth below as SEQ ID NOS 39 and 40:

SEQ ID NO. 39

ATGAATAAACGCGTAAAAATCGTTGCAACACTTGGTCCTGCGGTTGAATCCGTGGTGGTAAGAAGTT
TGGTGAGTCTGGATACTGGGGTGAAAGCCTTGACGTAGAAGCTTCAGCAGAAAAAATTGCTCAATTGA
TTAAAGAAGGTGCTAACGTTTTCCGTTTTCAACTTCTCACATGGAGATCATGCTGAGCAAGGAGCTCGT
ATGGCTACTGTTTCGTAAAGCAGAAGAGATTGCAGGACAAAAAGTTGGCTTCCTCCTTGATACTAAAGG
ACCTGAAATTCGTACAGAACTTTTTGAAGATGGTGCAGATTTCCATTCATATACAACAGGTACAAAAT
TACGTGTTGCTACTAAGCAAGGTATCAAATCAACTCCAGAAGTGATTGCATTGAATGTTGCTGGTGGTA
CTTGACATCTTTGATGACGTTGAAGTTGGTAAGCAAATCCTTGTTGATGATGGTAAACTAGGTCTTAC
TGTGTTTTGCAAAAGATAAAGACACTCGTGAATTTGAAGTAGTTGTTGAGAATGATGGCCTTATTGGTA
AACAAAAAGGTGTAAACATCCCTTATACTAAAATTCCTTTCCCAGCACTTGCAGAACGCGATAATGCT
GATATCCGTTTTGGACTTGAGCAAGGACTTAACTTTATTGCTATCTCATTGTACGTACTGCTAAAGA
TGTTAATGAAGTTCGTGCTATTTGTGAAGAACTGGSMATGGACACGTTAAGTTGTTTGCTAAAATTG
AAAATCAACAAGGTATCGATAATATTGATGAGATTATCGAAGCAGCAGATGGTATTATGATTGCTCGT
GGTGATATGGGTATCGAAGTTCATTTGAAATGGTTCCAGTTTACCAAAAAATGATCATTACTAAAGT
TAATGCAGCTGGTAAAGCAGTTATTACAGCAACAATATGCTTGAAACAATGACTGATAAACCACGTG
CGACTCGTTCAGAAGTATCTGATGTCTTCAATGCTGTTATTGATGGTACTGATGCTACAATGCTTTTCA
GGTGAGTCAGCTAATGGTAAATACCCAGTTGAGTCAGTTCGTACAATGGCTACTATTGATAAAAAATGC
TCAAACATTACTCAATGAGTATGGTCGCTTAGACTCATCTGCATTCCCACGTAATAACAAAACCTGATG
TTATTGCATCTGCGGTTAAAGATGCAACACTCAATGGATATCAAACCTTGTTGTAACAATTACTGAA
ACAGGTAATACAGCTCGTGCCATTTCTAAATTCCTGTCAGATGCAGACATTTTGGCTGTTACATTTGA
TGAAAAAGTACAACGTTCAATTGATGATTAACCTGGGGTGTATCCCTGTCCTTGACAGACAAACCAGCAT
CTACAGATGATATGTTTGAGGTTGCAGAACGTGTAGCACTTGAAGCAGGATTTGTTGAATCAGGCGAT
AATATCGTTATCGTTGCAGGTGTTCTGTAGGTACAGGTGGAACATAACAATGCGTGTTCTGCTACTGT
TAAA

SEQ ID NO. 40

MNKRVKIVATLGPAVEFRGGKKFGESGYWGESLDVEASAEKIAQLIKEGANVFRFNFSHGDHAEQGARG
 MATVRKAEIAGQKVGFLLDTKGPEIRTELFEDGADFHSYTTGTKLRVATKQGIKSTPEVIALNVAGG
 5 LDIFDDVEVGKQILVDDGKLGLTVFAKDKDTREFEVVVENDGLIGKQKGVNIPYTKIPFPALAERDNA
 DIRFGLEQGLNFIAISFVRTAKDVNEVRAICEETGXGHVKLFAKIENQQGIDNIDEIIEAADGIMIAR
 GDMGIEVPFEMVPVYQKMIITKVNAAGKAVITATNMLETMTDKPRATRSEVSDVFNAVIDGTDATMLS
 GESANGKYPVESVRTMATIDKNAQTLLNEYGRLDSSAFPRNNKTDVIASAVKDATHSMDIKLVVTITE
 10 TGNTARAI SKFRPDADILAVTFDEKVVQRSLMINWGVI PVLADKPASTDDMFEVAERVALEAGFVESGD
 NIVIVAGVPVGTGGTNTMRVRTVK

GBS 338

GBS 338 refers to a Sat D protein. Nucleotide and amino acid sequences of GBS 338
 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 8637 and SEQ
 15 ID 8638. These sequences are set forth below as SEQ ID NOS 41 and 42:

SEQ ID NO. 41

TTGTCTGCTATAATAGACAAAAAGGTGGTGATATTTATGTATTTAGCATTAAATCGGTGATATCATTAA
 TTCAAAACAGATACTTGAACGTGAAACTTTCCAACAGTCTTTTCAGCAACTAATGACCGAACTATCTG
 20 ATGTATATGGTGAAGAGCTGATTTCTCCATTCACTATTACAGCTGGTGATGAATTTCAAGCTTTATTG
 AAACCATCAAAAAAGGTATTTCAAATTATTGACCATATTCAACTAGCTCTAAAACCTGTTAATGTAAG
 GTTCGGCCTCGGTACAGGAAACATTATAACATCCATCAATTCAAATGAAAGTATCGGTGCTGATGGTC
 CTGCCTACTGGCATGCTCGCTCAGCTATTAATCATATACATGATAAAAATGATTATGGAACAGTTCAA
 GTAGCTATTTGCCTTGATGATGAAGACCAAAACCTTGAATTAACACTAAATAGTCTCATTTTCAGCTGG
 25 TGATTTTATCAAGTCAAAATGGACTACAAACCATTTTCAAATGCTTGAGCACTTAATACTTCAAGATA
 ATTATCAAGAACAATTTCAACATCAAAAGTTAGCCCAACTGGAAAAATATTGAACCTAGTGCGCTGACT
 AAACGCCTTAAAGCAAGCGGTCTGAAGATTTACTTAAGAACGAGAACACAGGCAGCCGATCTATTAGT
 TAAAAGTTGCACTCAAACATAAGGGGGAAGCTATGATTTT

SEQ ID NO. 42

MSAIIIDKKVVI FMYLALIGDI INSKQILERETFQQS FQQLMTELS DVYGEELISPFTITAGDEFQALL
 KPSKKVFQIIDHIQLALKPVNVRFLGTGNIIITSINSNESIGADGPAYWHARSAINHIHDKN DYGT VQ
 35 VAICLDDEDQNL ELTLNSLISAGDFIKSKWTTNHFQMLEHLILQDNYQE QFQHQKLAQLENIEPSALT
 KRLKASGLKIYLRTRTQAADLLVKSTQTKGGSYDF

GBS 338 may contain an N-terminal leader or signal sequence region which is indicated by
 the underlined sequence at the beginning of SEQ ID NO: 42 above. In one embodiment, one or more
 amino acids from the leader or signal sequence region are removed from GBS 338. An example of
 such a GBS 338 fragment is set forth below as SEQ ID NO: 43.

SEQ ID NO: 43

MYLALIGDI INSKQILERETFQQS FQQLMTELS DVYGEELISPFTITAGDEFQALLKPSKKVFQIIDH
 IQALALKPVNVRFLGTGNIIITSINSNESIGADGPAYWHARSAINHIHDKN DYGT VQVAICLDDEDQNL
 45 ELTLNSLISAGDFIKSKWTTNHFQMLEHLILQDNYQE QFQHQKLAQLENIEPSALT KRLKASGLKIYLR
 TRTQAADLLVKSTQTKGGSYDF

GBS 361

GBS 361 refers to a cyII protein. Nucleotide and amino acid sequences of GBS 361 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 8769 and SEQ ID 8770. These sequences are set forth below as SEQ ID NOS 44 and 45:

SEQ ID NO. 44

ATGAGCGTATATGTTAGTGGAATAGGAATTATTTCTTCTTTGGGAAAGAATTATAGCGAGCATAAACA
GCATCTCTTCGACTTAAAAGAAGGAATTTCTAAACATTTATATAAAAAATCACGACTCTATTTTAGAAT
CTTATACAGGAAGCATAACTAGTGACCCAGAGGTTCTTGAGCAATACAAAGATGAGACACGTAATTTT
10 AAATTTGCTTTTACCGCTTTTGAAGAGGCTCTTGCTTCTTCAGGTGTTAATTTAAAAGCTTATCATAA
TATTGCTGTGTGTTTAGGGACCTCACTTGGGGGAAAGAGTGCTGGTCAAAATGCCTTGTATCAATTTG
AAGAAGGAGAGCGTCAAGTAGATGCTAGTTTATTAGAAAAAGCATCTGTTTACCATATTGCTGATGAA
TTGATGGCTTATCATGATATTGTGGGAGCTTCGTATGTTATTTCAACCGCCTGTTCTGCAAGTAATAA
TGCCGTAATATTAGGAACACAATTACTTCAAGATGGCGATTGTGATTTAGCTATTTGTGGTGGCTGTG
15 ATGAGTTAAGTGATATTTCTTTAGCAGGCTTCACATCACTAGGAGCTATTAATACAGAAATGGCATGT
CAGCCCTATTCTTCTGGAAAAGGAATCAATTTGGGTGAGGGCGCTGGTTTTGTGTTCTTGTCAAAGA
TCAGTCCTTAGCTAAATATGGAAAATTATCGGTGGTCTTATTACTTCAGATGGTTATCATATAACAG
CACCTAAGCCAACAGGTGAAGGGGCGGCACAGATTGCAAAGCAGCTAGTGACTCAAGCAGGTATTGAC
TACAGTGAGATTGACTATATTAACGGTCACGGTACAGGTACTCAAGCTAATGATAAAATGGAAAAAAA
20 TATGTATGGTAAGTTTTTCCCGACAACGACATTGATCAGCAGTACCAAGGGGCAAACGGGTCACTC
TAGGGGCTGCAGGTATTATCGAATTGATTAATTGTTTAGCGGCAATAGAGGAACAGACTGTACCAGCA
ACTAAAAATGAGATTGGGATAGAAGGTTTTCCAGAAAATTTGTCTATCATCAAAAGAGAGAATACCC
AATAAGAAATGCTTTAAATTTTTTCGTTTGGTGAAATAATAGTGGTGTCTTATTGTCTATCTT
TAGATTCACCTCTAGAAACATTACCTGCTAGAGAAAATCTTAAATGGCTATCTTATCATCTGTTGCT
25 TCCATTTCTAAGAATGAATCACTTCTATAACCTATGAAAAAGTTGCTAGTAATTTCAACGACTTTGA
AGCATTACGCTTTAAAGGGGCTAGACCACCCAAAACGTCAACCCAGCACAAATTTAGGAAAATGGATG
ATTTTTCCAAAATGGTTGCCGTAACAACAGCTCAAGCACTAATAGAAAGCAATATTAATCTAAAAAAA
CAAGATACTTCAAAGTAGGAATTGTATTTACAACACTTCTGGACCAGTTGAGGTTGTTGAAGGTAT
TGAAAAGCAAATCACAACAGAAGGATATGCACATGTTTCTGCTTCACGATTCCCGTTTACAGTAATGA
30 ATGCAGCAGCTGGTATGCTTTCTATCATTTTTTAAATAACAGGTCCTTTATCTGTCAATTCGACAAAT
AGTGGAGCGCTTGATGGTATACAATATGCCAAGGAAATGATGCGTAACGATAATCTAGACTATGTGAT
TCTTGTTTCTGCTAATCAGTGGACAGACATGAGTTTTATGTGGTGGCAACAATTAACATATGATAGTC
AAATGTTTGTGCGTTCTGATTATGTTTCAGCACAAAGTCCTCTCTCGTCAAGCATTGGATAATTTCTCCT
ATAATATTAGGTAGTAAACAATTAATAATATAGCCATAAAACATTCACAGATGTGATGACTATTTTTGA
35 TGCTGCGCTTCAAATTTATTATCAGACTTAGGACTAACCATAAAAGATATCAAAGGTTTCGTTTGGG
ATGAGCGGAAGAAGGCAGTTAGTTCAGATTATGATTTCTTAGCGAACTTGTCTGAGTATTATAATATG
CCAAACCTTGCTTCTGGTCAGTTTGGATTTTCATCTAATGGTGTCTGGTGAAGAAGTGGACTATACTGT
TAATGAAAGTATAGAAAAGGGCTATTATTTAGTCCTATCTTATTCGATCTTCGGTGGTATCTCTTTTG
CTATTATTGAAAAAAGG

SEQ ID NO. 45

MSVYVSGIGIISSLGKNYSEHKQHLFDLKEGISKHLYKNHDSILES YTGSI TSDPEVPEQYKDETRNF
KFAFTAFEEALASSGVNLKAYHNIAVCLGTS LGGKSAGQNALYQFEEGERQVDASLLEKASVYHIAD E
LMAYHDI VGASYVISTACSASNNAVILGTQLLQDGDCLAI CGGCD ELSDISLAGFTSLGAINTEMAC
45 QPYSSGKGINLGE GAGFVVLVKDQSLAKYGKIIGGLITSDGYHITAPKPTGEGAAQIAKQLVTQAGID
YSEIDYINGHGTGTQANDKMEKNMYGKFFPTTTLISSTKGQTGHTLGAAGIIE LINCLAAIEEQTVPA
TKNEIGIEGF PENFVYHQKREYPIRNALNFSFAFGGNSGVLLSSLDSPLETLPAREN LKMAILSSVA
SISKNESLSITYEKVASNFNDFEALRFKGARPPKTVNPAQFRKMDDFSKMVAVTTAQALIESNINLKK
QDTSKVGIVFTT LSGPVEVVEGIEKQITTEGYAHVSASRFPFTVMNAAAGMLSIIIFKITGPLSVISTN
50 SGALDGIQYAKEMMRNDNLDYVILV SANQWTDMSFMWWQQLNYDSQMFVGS DYCSAQVLSRQALDNSP

I I L G S K Q L K Y S H K T F T D V M T I F D A A L Q N L L S D L G L T I K D I K G F V W N E R K K A V S S D Y D F L A N L S E Y Y N M
P N L A S G Q F G F S S N G A G E E L D Y T V N E S I E K G Y Y L V L S Y S I F G G I S F A I I E K R

GBS 361 may contain an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO: 45 above. In one embodiment, one or more amino acids from the leader or signal sequence region are removed from GBS 361. An example of such a GBS 361 fragment is set forth below as SEQ ID NO: 46.

SEQ ID NO: 46

V S G I G I I S S L G K N Y S E H K Q H L F D L K E G I S K H L Y K N H D S I L E S Y T G S I T S D P E V P E Q Y K D E T R N F K F A F
T A F E E A L A S S G V N L K A Y H N I A V C L G T S L G G K S A G Q N A L Y Q F E E G E R Q V D A S L L E K A S V Y H I A D E L M A Y
H D I V G A S Y V I S T A C S A S N N A V I L G T Q L L Q D G D C D L A I C G G C D E L S D I S L A G F T S L G A I N T E M A C Q P Y S
S G K G I N L G E G A G F V V L V K D Q S L A K Y G K I I G G L I T S D G Y H I T A P K P T G E G A A Q I A K Q L V T Q A G I D Y S E I
D Y I N G H G T G T Q A N D K M E K N M Y G K F F P T T L I S S T K G Q T G H T L G A A G I I E L I N C L A A I E E Q T V P A T K N E
I G I E G F P E N F V Y H Q K R E Y P I R N A L N F S F A F G G N S G V L L S S L D S P L E T L P A R E N L K M A I L S S V A S I S K
N E S L S I T Y E K V A S N F N D F E A L R F K G A R P P K T V N P A Q F R K M D D F S K M V A V T T A Q A L I E S N I N L K K Q D T S
K V G I V F T T L S G P V E V E G I E K Q I T T E G Y A H V S A S R F P F T V M N A A A G M L S I I F K I T G P L S V I S T N S G A L
D G I Q Y A K E M M R N D N L D Y V I L V S A N Q W T D M S F M W W Q Q L N Y D S Q M F V G S D Y C S A Q V L S R Q A L D N S P I I L G
S K Q L K Y S H K T F T D V M T I F D A A L Q N L L S D L G L T I K D I K G F V W N E R K K A V S S D Y D F L A N L S E Y Y N M P N L A
S G Q F G F S S N G A G E E L D Y T V N E S I E K G Y Y L V L S Y S I F G G I S F A I I E K R

GBS 404

Nucleotide and amino acid sequences of GBS 404 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 8799 and SEQ ID 8800. These sequences are set forth below as SEQ ID NOS 47 and 48:

SEQ ID NO. 47

A T G A A A A T A G A T G A C C T A A G A A A A A G C G A C A A T G T T G A A G A T C G T C G C T C C A G T A G C G G A G G T T C A T T
C T C T A G C G G A G G A A G T G G A T T A C C G A T T C T T C A A C T T T T A T T G C T G C G A G G G A G T T G G A A A C C A A G C
T T G T G G T T T T A A T C A T C T T A C T G C T A C T T G G C G G A G G G G A C T A A C C A G C A T T T T T A A T G A C T C A T C C
T C A C C T T C T A G T T A C C A A T C T C A G A A T G T C T C A C G T T C T G T T G A T A A T A G C G C A A C G A G A G A A C A A A T
C G A T T T C G T T A A T A A A G T C C T T G G C T C A A C T G A G G A T T T C T G G T C A C A A G A A T T C C A A C C C A A G G T T
T T G G A A A T T A T A A G G A A C C A A A A C T T G T T C T T T A C A C C A A T T C A A T T C A A C A G G T T G T G G T A T A G G T
G A A T C T G C T T C A G G A C C A T T T T A T T G T T C A G C A G A T A A A A A A T C T A T C T T G A T A T T T C T T T T T A C A A
T G A A T T A T C A C A T A A A T A T G G T G C T A C T G G T G A T T T T G C T A T G G C C T A C G T C A T C G C C C A C G A A G T T G
G T C A C C A C A T T C A A C A G A G T T A G G C A T T A T G G A T A A G T A T A A T A G A A T G C G A C A C G G A C T T A C T A A G
A A A G A A G C A A A T G C T T T A A A T G T T C G G C T A G A A C T T C A A G C A G A T T A T T A T G C A G G G G T A T G G G C T C A
C T A C A T C A G G G G A A A A A T C T C T T A G A A C A A G G A G A C T T T G A A G A G G C C A T G A A T G C T G C C C A C G C C G
T C G G A G A C G A T A C C C T T C A G A A A G A A C C T A C G G A A A A T T A G T G C C T G A T A G C T T T A C C C A T G G A A C A
G C T G A A C A A C G C C A A C G T T G G T T T A A C A A A G G C T T T C A A T A T G G T G A C A T C C A A C A C G G T G A T A C T T T
C T C C G T A G A A C A T C T A

SEQ ID NO. 48

M K I D D L R K S D N V E D R R S S S G G S F S S G G S G L P I L Q L L L L R G S W K T K L V V L I I L L L L G G G G L T S I F N D S S
S P S S Y Q S Q N V S R S V D N S A T R E Q I D F V N K V L G S T E D F W S Q E F Q T Q G F G N Y K E P K L V L Y T N S I Q T G C G I G
E S A S G P F Y C S A D K K I Y L D I S F Y N E L S H K Y G A T G D F A M A Y V I A H E V G H H I Q T E L G I M D K Y N R M R H G L T K
K E A N A L N V R L E L Q A D Y Y A G V W A H Y I R G K N L L E Q G D F E E A M N A A H A V G D D T L Q K E T Y G K L V P D S F T H G T
A E Q R Q R W F N K G F Q Y G D I Q H G D T F S V E H L

GBS 690

Nucleotide and amino acid sequences of GBS 690 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 9965 and SEQ ID 9966. These sequences are set forth as
 5 SEQ ID NOS 49 and 50 below:

SEQ ID NO. 49

ATGAGTAAACGACAAAATTTAGGAATTAGTAAAAAAGGAGCAATTATATCAGGGCTCTCAGTGGCACT
 AATTGTAGTAATAGGTGGCTTTTTATGGGTACAATCTCAACCTAATAAGAGTGCAGTAAAACTAACT
 10 ACAAAGTTTTTAATGTTAGAGAAGGAAGTGTTCGTCCTCAACTCTTTTGACAGGAAAAGCTAAGGCT
 AATCAAGAACAGTATGTGTATTTTGATGCTAATAAAGGTAATCGAGCAACTGTCACAGTTAAAGTGGG
 TGATAAAATCACAGCTGGTCAGCAGTTAGTTCAATATGATACAACAACTGCACAAGCAGCCTACGACA
 CTGCTAATCGTCAATTAAATAAAGTAGCGCGTCAGATTAATAATCTAAAGACAACAGGAAGTCTTCCA
 15 GCTATGGAATCAAGTGATCAATCTTCTTCATCATCACAAGGACAAGGGACTCAATCGACTAGTGGTGC
 GACGAATCGTCTACAGCAAAATTATCAAAGTCAAGCTAATGCTTCATACAACCAACAACCTTCAAGATT
 TGAATGATGCTTATGCAGATGCACAGGCAGAAAGTAAATAAAGCACAAAAAGCATTGAATGATACTGTT
 ATTACAAGTGACGTATCAGGGACAGTTGTTGAAGTTAATAGTGATATTGATCCAGCTTCAAAAACCTAG
 TCAAGTACTTGTCCATGTAGCAACTGAAGGTAACTCCAAGTACAAGGAACGATGAGTGAGTATGATT
 TGGCTAATGTTAAAAAAGACCAGGCTGTTAAAATAAAATCTAAGGTCTATCCTGACAAGGAATGGGAA
 20 GGTAAAATTTTATATATCTCAAATTATCCAGAAGCAGAAGCAAACAACAATGACTCTAATAACGGCTC
 TAGTGCTGTAAATTATAAATATAAAGTAGATATTACTAGCCCTCTCGATGCATTAACAAGGTTTTTA
 CCGTATCAGTTGAAGTAGTTAATGGAGATAAGCACCTTATTGTCCCTACAAGTTCTGTGATAAACAAA
 GATAATAAACACTTTTGTGGGTATACAATGATTCTAATCGTAAATTTTCCAAAGTTGAAGTCAAAAT
 TGGTAAAGCTGATGCTAAGACACAAGAAATTTTATCAGGTTTGAAAGCAGGACAAATCGTGGTTACTA
 25 ATCCAAGTAAAACCTTCAAGGATGGGCAAAAATTTGATAATATTGAATCAATCGATCTTAACTCTAAT
 AAGAAATCAGAGGTGAAA

SEQ ID NO. 50

MSKRQNLGISKKGAIISGLSVALIVVIGGFLWVQSQPNKSAVKTNKYKVFNVREGSVSSSTLLTGKAKA
 30 NQEQYVYFDANKGNRATVTVKVGDKITAGQQLVQYDTTTAQAAAYDTANRQLNKVARQINNLTGSLP
 AMESSDQSSSSSQGGTQSTSGATNRLQQNYQSQANASYNQQLQDLNDAYADAQAEVNKAQKALNDTV
 ITSDVSGTVVEVNSDIDPASKTSQVLVHVATEGKLQVQGTMSSEYDLANVKKDQAVKIKSKVYPDKWEW
 GKISYISNYPEAEANNNDSSNGSSAVNYKYKVDITSPDLALKQGFVTSVEVVNGDKHLIVPTSSVINK
 DNKHFVWVYNDNSNRKISKVEVKIGKADAKTQEILSGLKAGQIVVTNPSKTFKDGQKIDNIESIDLNSN
 35 KKSEVK

GBS 690 contains an N-terminal leader or signal sequence region which is indicated by the
 underlined sequence at the beginning of SEQ ID NO: 50 above. In one embodiment, one or more
 amino acids from the leader or signal sequence region of GBS 690 are removed. An example of such
 40 a GBS 690 fragment is set forth below as SEQ ID NO: 51.

SEQ ID NO: 51

FLWVQSQPNKSAVKTNKYKVFNVREGSVSSSTLLTGKAKANQEQYVYFDANKGNRATVTVKVGDKITAG
 45 QQLVQYDTTTAQAAAYDTANRQLNKVARQINNLTGSLPAMESSDQSSSSSQGGTQSTSGATNRLQQ
 NYQSQANASYNQQLQDLNDAYADAQAEVNKAQKALNDTVITSDVSGTVVEVNSDIDPASKTSQVLVHV
 ATEGKLQVQGTMSSEYDLANVKKDQAVKIKSKVYPDKEWEGKISYISNYPEAEANNNDSSNGSSAVNYK
 YKVDITSPDLALKQGFVTSVEVVNGDKHLIVPTSSVINKDNKHFVWVYNDNSNRKISKVEVKIGKADAK
 TQEILSGLKAGQIVVTNPSKTFKDGQKIDNIESIDLNSNKKSEVK

GBS 691

GBS 691 refers to an iron compound ABC transporter, or a substrate binding protein.

Nucleotide and amino acid sequences of GBS 691 sequenced from serotype V isolated strain 2603

- 5 V/R are set forth in Ref. 2 as SEQ ID 3691 and SEQ ID 3692. These sequences are set forth as SEQ ID NOS 52 and 53 below:

SEQ ID NO. 52

ATGAAAAAATTGGAATTATTGTCCTCACACTACTGACCTTCTTTTTGGTATCTTGCGGACAACAAAC
 10 TAAACAAGAAAGCACTAAAACAACCTATTTCTAAAATGCCTAAAATGAAGGCTTCACCTATTATGGAA
 AAATTCCTGAAAATCCGAAAAAGTAATTAATTTTACATATTCTTACACTGGGTATTTATTAATACTA
 GGTGTTAATGTTTCAAGTTACAGTTTAGACTTAGAAAAAGATAGCCCCGTTTTTGGTAAACAACCTGAA
 AGAAGCTAAAAAATTAAGTCTGATGATACAGAAGCTATTGCCGCACAAAAACCTGATTTAATCATGG
 TTTTCGATCAAGATCCAAACATCAATACTCTGAAAAAATTCACCAACTTTAGTTATTAAATATGGT
 15 GCACAAAATTATTTAGATATGATGCCAGCCTTGGGGAAAGTATTCGGTAAAGAAAAAGAAGCTAATCA
 GTGGGTAGCCAATTGGAATAAACTCTCGCTGTCAAAAAAGATTTACACCATATCTTAAAGCCTA
 AACTACTTTTACTATTATGGATTTTTATGATAAAAAATATCTATTATATGTAATAATTTTGGACGC
 GGTGGAGAATAATCTATGATTCAGGTTATGCTGCCCCAGAAAAAGTCAAAAAAGATGTCTTTAA
 AAAAGGGTGGTTTACCGTTTCGCAAGAAGCAATCGGTATTACGTTGGAGATTATGCCCTTGTTAATA
 TAAACAAAACGACTAAAAAAGCAGCTTCATCACTTAAAGAAAGTGATGTCTGGAAGAATTTACCAGCT
 20 GTCAAAAAAGGGCACATCATAGAAAGTAACTACGACGTGTTTTATTTCTCTGACCCTCTATCTTTAGA
 AGCTCAATTAAATCATTTACAAAGGCTATCAAAGAAAATACAAAT

SEQ ID NO. 53

MKKIGIIVLTLLTFFLVSCGQQTQESTKTTISKMPKIEGFTYYGKIPENPKKVINFYTSYTGYYLLKL
 25 GNVSSYSLDLEKDSPVFGKQLKEAKKLTADDTEAIAAQKPDLMVFDQDPNINTLKKIAPTLVIKYG
 AQNYLDMMPALGKVFGKEKEANQWVSQWKTKTLAVKKDLHHILKPNTTFTIMDFYDKNIYLYGNNFGR
 GGELIYDSLGYAAPEKVKKDVFKKGWFTVSQEAIGDYVGDYALVNINKTTKKAASSLKESDVWKNLPA
 VKKGHIIESNYDVFFYFSDPLSLEAQLKSFTKAIKENTN

- 30 GBS 691 contains an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO: 53 above. In one embodiment, one or more amino acids are removed from the leader or signal sequence region of GBS 691. An example of such a GBS 691 fragment is set forth below as SEQ ID NO: 54.

SEQ ID NO: 54

EGFTYYGKIPENPKKVINFYTSYTGYYLLKLGNVSSYSLDLEKDSPVFGKQLKEAKKLTADDTEAIAA
 35 QKPDLMVFDQDPNINTLKKIAPTLVIKYGAQNYLDMMPALGKVFGKEKEANQWVSQWKTKTLAVKKD
 LHHLKPNTTFTIMDFYDKNIYLYGNNFGRGGELIYDSLGYAAPEKVKKDVFKKGWFTVSQEAIGDYV
 40 GDYALVNINKTTKKAASSLKESDVWKNLPAVKKGHIIESNYDVFFYFSDPLSLEAQLKSFTKAIKENTN

GBS 691 contains a C-terminal transmembrane or cytoplasmic region which is indicated by the underlined sequence at the end of SEQ ID NO: 53 above. In one embodiment, one or more amino acids are removed from the transmembrane or cytoplasmic region of GBS 691. An example of such a GBS 691 fragment is set forth below as SEQ ID NO: 55.

SEQ ID NO: 55

MKKI GIIVL TLLTFFLVSCGQQTKESTKTTISKMPKIEGFTYYGKIPENPKKVINFYTSYTGYYLLKL
 GNVNSSSYSLDLEKDSPVFGKQLKEAKKLTADDTEAIAAQKPDLMVFDQDPNINTLKKIAPTLVIKYG
 AQNYLDMMPALGKVFGKEKEANQWVSQWKTKTLAVKKDLHHILKPNTTFTIMDFYDKNIYLYGNNFGR
 5 GGELIYDSLGYAAPEKVKKDVFKKGWFTVSQEAIGDYVGDYALVNINKTTKKAASSLKESDVWKNLPA
 VKKGHIIESNYDVFFYFSDPLSLEAQLKSFT

In one embodiment, one or more amino acids from the leader or signal sequence region and
 one or more amino acids from the transmembrane or cytoplasmic region are removed from GBS 691.

One example of such a GBS 691 fragment is set forth below as SEQ ID NO: 56

SEQ ID NO: 56

EGFTYYGKIPENPKKVINFYTSYTGYYLLKLGNVSSSYSLDLEKDSPVFGKQLKEAKKLTADDTEAIAA
 QKPDLMVFDQDPNINTLKKIAPTLVIKYGAQNYLDMMPALGKVFGKEKEANQWVSQWKTKTLAVKKD
 15 LHHILKPNTTFTIMDFYDKNIYLYGNNFGRGGELIYDSLGYAAPEKVKKDVFKKGWFTVSQEAIGDYV
 GDYALVNINKTTKKAASSLKESDVWKNLPAVKKGHIIESNYDVFFYFSDPLSLEAQLKSFT

Additional examples of GBS antigens which may be used in combination with GBS 80 are set
 forth below.

GBS 4

GBS 4 refers to another putative cell wall surface anchor family protein. Nucleotide and
 amino acid sequences of GBS 4 sequenced from serotype V isolated strain 2603 V/R are set forth in
 Ref. 2 as SEQ ID 1 and SEQ ID 2. These sequences are also set forth below as SEQ ID NOS 57 and
 58:

SEQ ID NO. 57

ATGAAAGTGAAAAATAAGATTTTAACGATGGTAGCACTTACTGTCTTAACATGTGCTACTTATTCATC
 AATCGGTTATGCTGATACAAAGTGATAAGAATACTGACACGAGTGTCTGACTACGACCTTATCTGAGG
 AGAAAAGATCAGATGAAC TAGACCAGTCTAGTACTGGTTCTTCTTCTGAAAATGAATCGAGTTCATCA
 30 AGTGAACCAGAAACAAATCCGTCAACTAATCCACCTACAACAGAACCATCGCAACCCTCACCTAGTGA
 AGAGAACAAGCCTGATGGTAGAACGAAGACAGAAATTGGCAATAATAAGGATATTTCTAGTGGAACAA
 AAGTATTAATTTTCAGAAGATAGTATTAAGAATTTTAGTAAAGCAAGTAGTGATCAAGAAGAAGTGGAT
 CGCGATGAATCATCATCTTCAAAAGCAAATGATGGGAAAAAAGGCCACAGTAAGCCTAAAAAGGAACT
 TCCTAAAACAGGAGATAGCCACTCAGATACTGTAATAGCATCTACGGGAGGGATTATTCTGTTATCAT
 35 TAAGTTTTTTACAATAAGAAAATGAACTTTAT

SEQ ID NO. 58

MKVKNKILTMVALTVLTCATYSSIGYADTSDKNTDTSVVTTTLSEEKRSDELDQSSTGSSSENESSSS
 SEPETNPSTNPPTTEPSQPSPEENKPDGRTEIGNNKDISSGTVLISEDSEIKNFSKASSDQEEVD
 40 RDESSSSKANDGKKGHSKPKKELPKTGDSHSDTVIASTGGIILLSLSFYNKKMKLY

GBS 4 contains an N-terminal leader or signal sequence which is underlined at the beginning
 of SEQ ID NO: 58 above. In one embodiment, one or more amino acids from the N-terminal leader
 or signal peptide domain of GBS 4 are removed. An example of such a GBS 4 fragment is set forth
 45 below as SEQ ID NO 59.

SEQ ID NO 59

DTSDKNTDTSVVTTLSEEKRSDEL DQSSTGSSSENESSSSSEPETNPSTNPPTTEPSQSPSEENKP
DGR TKTEIGNNKDISSG TKVLISED S IKNFSKASSDQEEVDRDESSSSKANDGKKGH SKPKKELPKTG
DSHSDTVIASTGGIILL SLSFYNNKMKLY

5

A further N-terminal section of GBS 4 may be removed to facilitate recombinant expression.
An example of such a GBS 4 fragment is set forth below as SEQ ID NO: 60.

SEQ ID NO: 60

10 DQSSTGSSSENESSSSSEPETNPSTNPPTTEPSQSPSEENKPDGR TKTEIGNNKDISSG TKVLISED
S IKNFSKASSDQEEVDRDESSSSKANDGKKGH SKPKKELPKTGDSHSDTVIASTGGIILL SLSFYNNK
MKLY

GBS 4 contains an C-terminal transmembrane region which is underlined at the end of SEQ
15 ID NO: 58 above. In one embodiment, one or more amino acids from the C-terminal transmembrane
region is removed. An example of such a GBS 4 fragment is set forth below as SEQ ID NO: 61.

SEQ ID NO: 61

20 MKVKNKILTMVALTVLT CATYSSIGYADTSDKNTDTSVVTTLSEEKRSDEL DQSSTGSSSENESSSS
SEPETNPSTNPPTTEPSQSPSEENKPDGR TKTEIGNNKDISSG TKVLISED S IKNFSKASSDQEEVD
RDESSSSKANDGKKGH SKPKKE

In one embodiment, both the N-terminal leader or signal domain and the C-terminal
transmembrane domain are removed from the GBS 4 sequence. An example of such a GBS 4
25 fragment is set forth below as SEQ ID NO: 62.

SEQ ID NO: 62

30 DTSDKNTDTSVVTTLSEEKRSDEL DQSSTGSSSENESSSSSEPETNPSTNPPTTEPSQSPSEENKP
DGR TKTEIGNNKDISSG TKVLISED S IKNFSKASSDQEEVDRDESSSSKANDGKKGH SKPKKE

In yet another embodiment, the N-terminal leader or signal domain, a further N-terminal
region and the C-terminal transmembrane domain are removed from the GBS 4 sequence. An
example of such a GBS 4 fragment is set forth below as SEQ ID NO: 63.

SEQ ID NO: 63

35 DQSSTGSSSENESSSSSEPETNPSTNPPTTEPSQSPSEENKPDGR TKTEIGNNKDISSG TKVLISED
S IKNFSKASSDQEEVDRDESSSSKANDGKKGH SKPKKE

GBS 22

40 GBS 22 refers to a putative adhesion lipoprotein. Nucleotide and amino acid sequences of
GBS 22 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ 8583 and
SEQ ID 8584. These sequences are set forth below as SEQ ID NOS 64 and 65:

SEQ ID NO. 64

ATGAAAAGGATACGGAAAAGCCTTATTTTTGTTCTCGGAGTAGTTACCCTAATTTGCTTATGTGCTTG
 TACTAAACAAAGCCAGCAAAAAAATGGCTTGTCAGTAGTGACTAGCTTTTATCCAGTATATTCCATTA
 CAAAAGCAGTTTCTGGTGATTGAATGATATTAATGATTTCGATCACAGTCAGGTATTCATGGTTTT
 5 GAACCTCATCAAGTGATGTTGCTGCCATTTATGATGCTGATCTATTTCTTTATCATTGCGCACACT
 AGAAGCTTGGGCGAGACGTTTGAACCTAGTTTGCATCACTCTAAAGTATCTGTAATTGAAGCTTCAA
 AAGGTATGACTTTGGATAAAGTTCATGGCTTAGAAGATGTAGAGGCAGAAAAAGGAGTAGATGAGTCA
 ACCTTGTATGACCCTCACACTTGAATGACCCTGTAAAAGTATCTGAGGAAGCACAACTCATCGCTAC
 ACAATTAGCTAAAAAGGATCCTAAAAACGCTAAGGTTTATCAAAAAAATGCTGATCAATTTAGTGACA
 10 AGGCAATGGCTATTGCAGAGAAGTATAAGCCAAAATTTAAAGCTGCAAAGTCTAAATACTTTGTGACT
 TCACATACAGCATTCTCATACTTAGCTAAGCGATACGGATTGACTCAGTTAGGTATTGCAGGTGTCTC
 AACC GAGCAAGAACCTAGTGCTAAAAAATTAGCCGAAATTCAGGAGTTTGTGAAAACATATAAGGTTA
 AGACTATTTTTTGTGTAAGAAGGAGTCTCACCTAAATTAGCTCAAGCAGTAGCTTCAGCTACTCGAGTT
 AAAATTGCAAGTTTAAAGTCTTTARAAGCAGTTCCCAAAAACAATAAAGATTACTTAGAAAATTTGGA
 15 AACTAATCTTAAGGTACTTGTCAAATCGTTAAATCAATAG

SEQ ID NO. 65

MKRIRKSLIFVLGVVTLICLCACTKQSQQKNGLSVVTSFYVPVYSITKAVSGDLNDIKMIRSQSGIHGF
 EPSSSDVAAYIDADLFYHSHTLEAWARRLEPSLHHSKVSVIEASKGMTLDKVHGLEDEAEKGVDES
 20 TLYDPHTWNDPVKVSEEAQLIATQLAKKDPKNAKVYQKNADQFSDKAMAI AEKYKPKFKAAKSKYFVT
 SHTAFSYLAKRYGLTQLGIAGVSTEQEPSAKKLAEIQEFVKTYKVKTIFVEEGVSPKLAQAVASATRV
 KIASLSPLXAVPKNNKDYLENLETNLKVLVKSLNQ

GBS 85

25 GBS 85 refers to a putative cell division protein (DivIB). Nucleotide and amino acid
 sequences of GBS 85 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as
 SEQ ID 215 and SEQ ID 216. These sequences are set forth below as SEQ ID NOS 66 and 67:

SEQ ID NO. 66

30 ATGCCTAAGAAGAAATCAGATACCCCAGAAAAAGAAGAAGTTGTCTTAACGGAATGGCAAAAAGCGTAA
 CCTTGAATTTTTTAAAAAACGCAAAGAAGATGAAGAAGAACAAAAACGTATTAACGAAAAATTACGCT
 TAGATAAAAGAAGTAAATTAATATTTCTTCTCCTGAAGAACCTCAAATACTACTAAAAATTAAGAAG
 CTTCATTTTTCCAAAGATTTCAAGACCTAAGATTGAAAAGAAACAGAAAAAAGAAAAAATAGTCAACAG
 CTTAGCCAAAATAATCGCATTAGAAGTGCACCTATATTTGTAGTAGCATTCTAGTCATTTTAGTTT
 35 CCGTTTTCTACTAACTCCTTTTAGTAAGCAAAAACAATAACAGTTAGTGGAAATCAGCATAACCT
 GATGATATTTTGTAGAGAAAACGAATATTCAAAAAACGATTATTTCTTTTCTTTAATTTTTTAAACA
 TAAAGCTATTGAACAACGTTTAGCTGCAGAAGATGTATGGGTAAAAACAGCTCAGATGACTTATCAAT
 TTCCCAATAAGTTTCATATTCAAGTTCAAGAAAATAAGATTATTGCATATGCACATACAAAGCAAGGA
 TATCAACCTGTCTTGGAACTGGAAAAAAGGCTGATCCTGTAAATAGTTCAGAGCTACCAAAGCACTT
 40 CTTAACAATTAACCTTGATAAGGAAGATAGTATTAAGCTATTAATTAAAGATTAAAGGCTTTAGACC
 CTGATTTAATAAGTGAGATTGAGGTGATAAGTTTAGCTGATTCTAAAACGACACCTGACCTCCTGCTG
 TTAGATATGCACGATGGAAATAGTATTAGAATACCATTATCTAAATTTAAAGAAAGACTTCCTTTTTTA
 CAAACAAATTAAGAAGAACCTTAAGGAACCTTCTATTGTTGATATGGAAGTGGGAGTTTACACAACAA
 CAAATACCATTGAATCAACCCCTGTAAAGCAGAAGATACAAAAATAAATCAACTGATAAAACACAA
 45 ACACAAAATGGTCAGGTTGCGGAAAATAGTCAAGGACAAACAAATAACTCAAATACTAATCAACAAGG
 ACAACAGATAGCAACAGAGCAGGCACCTAACCTCAAATGTTAAT

SEQ ID NO. 67

50 MPKKKSDTPEKEEVVLTEWQKRNLEFLKKRKEDEEEQKRINEKLRLDKRSKLNISPEEPQNTTKIKK
 LHF PKISRPKIEKKQKKEKIVNSLAKTNRI RTAPIFVVAFLVILVSFLLTPFSKQKTITVSGNQHTP
 DDILIEKTNIQKNDYFFSLIFKHKAIEQRLAAEDVWVKTAQMTYQFPNKFHIQVQENKIIAYAHTKQG

YQPVLETGKKADPVNSSELPKHFLTINLDKEDSIKLLIKDLKALDPDLISEIQVISLADSKTTPDLLL
LDMHDGNSIRIPLSKFKERLPFYKQIKKNLKEPSIVDMEVGVYTTTNTIESTPVKAEDTKNKSTDKTQ
TQNGQVAENSQGQTNNSTNTNQQGQQIATEQAPNPQNVN

5 **GBS 147**

GBS 147 refers to a putative protease. Nucleotide and amino acid sequences of GBS 147 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 8525 and SEQ ID 8526. These sequences are set forth below as SEQ ID NOS 68 and 69.

10 **SEQ ID NO. 68**

GTGGATAAACATCACTCAAAAAAGGCTATTTTAAAGTTAACTTATAACAACCTAGTATTTTATTAAT
GCATAGCAATCAAGTGAATGCAGAGGAGCAAGAATTAACCAAGAGCAATCACCTGTAATTGCTA
ATGTTGCTCAACAGCCATCGCCATCGGTAACCTACTAATACTGTTGAAAAACATCTGTAACAGCTGCT
15 TCTGCTAGTAATACAGCGAAAGAAATGGGTGATACATCTGTAAAAAATGACAAAACAGAAGATGAATT
ATTAGAAGAGTTATCTAAAAACCTTGATACGTCTAATTTGGGGGCTGATCTTGAAGAAGAATATCCCT
CTAAACCAGAGACAACCAACAATAAAGAAAGCAATGTAGTAACAAATGCTTCAACTGCAATAGCACAG
AAAGTTCCCTCAGCATATGAAGAGGTGAAGCCAGAAAGCAAGTCATCGCTTGCTGTTCTTGATACATC
TAAAATAACAAAATTACAAGCCATAACCCAAAGAGGAAAGGGAAATGTAGTAGCTATTATTGATACTG
20 GCTTTGATATTAACCATGATATTTTCGTTTAGATAGCCCAAAGATGATAAGCACAGCTTTAAACT
AAGACAGAATTTGAGGAATTAAGCAAAACATAATATCACTTATGGGAAATGGGTTAACGATAAGAT
TGTTTTTGCACATAACTACGCCAACAATACAGAAACGGTGGCTGATATTGCAGCAGCTATGAAAGATG
GTTATGGTTCAGAAGCAAAGAATATTTTCGCATGGTACACACGTTGCTGGTATTTTGTAGGTAATAGT
AAACGTCCAGCAATCAATGGTCTTCTTTTGAAGGTGCAGCGCCAAATGCTCAAGTCTTATTAATGCG
TATTCCAGATAAAATTGATTTCGGACAAATTTGGTGAAGCATATGCTAAAGCAATCACAGACGCTGTTA
25 ATCTAGGAGCAAAAACGATTAATATGAGTATTGAAAAACAGCTGATTCTTTAATTGCTCTCAATGAT
AAAGTTAAATTAGCACTTAAATTAGCTTCTGAGAAGGGCGTTGCAGTTGTTGTGGCTGCCGGAATGA
AGGCGCATTTGGTATGGATTATAGCAAACCATTAACAATACTGACTACGGTACGGTTAATAGTC
CAGCTATTTCTGAAGATACTTTGAGTGTTGCTAGCTATGAATCACTTAAACTATCAGTGAGGTCGTT
GAAACAACCTATTGAAGGTAAGTTAGTTAAGTTGCCGATTGTGACTTCTAAACCTTTTGACAAAGGTAA
30 GGCCTACGATGTGGTTTATGCCAATTATGGTGCAAAAAAAGACTTTGAAGGTAAGGACTTTAAAGGTA
AGATTGCATTAATTGAGCGTGGTGGTGGACTTGATTTTATGACTAAAATCACTCATGCTACAAATGCA
GGTGTGTTGGTATCGTTATTTTTAACGATCAAGAAAAACGTGGAAATTTTCTAATTCCTTACCGTGA
ATTACCTGTGGGATTATTAGTAAAGTAGATGGCGAGCGTATAAAAAATACTTCAAGTCAGTTAACAT
TTAACCAGAGTTTGAAGTAGTTGATAGCCAAGGTGTAATCGTATGCTGGAACAATCAAGTTGGGGC
35 GTGACAGCTGAAGGAGCAATCAAGCCTGATGTACAGCTTCTGGCTTGAATTTATTCCTCAACCTA
TAATAATCAATACCAACAATGTCTGGTACAAGTATGGCTTACCACATGTTGCAGGATTAATGACAA
TGCTTCAAAGTCATTTGGCTGAGAAATATAAAGGGATGAATTTAGATTCTAAAAAATTGCTAGAATTG
TCTAAAAACATCCTCATGAGCTCAGCAACAGCATTATATAGTGAAGAGGATAAGGCGTTTTATTCCACC
ACGTCAGCAAGGTGCAGGTGTAGTTGATGCTGAAAAAGCTATCCAAGCTCAATATTATATTACTGGAA
40 ACGATGGCAAAGCTAAATTAATCTCAAACGAATGGGAGATAAATTTGATATCACAGTTACAATTCAT
AACTTGTAGAAGGTGTCAAAGAATTGTATTATCAAGCTAATGTAGCAACAGAACAAGTAAATAAAGG
TAAATTTGCCCTTAAACCACAAGCCTTGCTAGATACTAATTGGCAGAAAGTAATTCCTTCGTGATAAAG
AAACACAAGTTCGATTTACTATTGATGCTAGTCAATTTAGTCAGAAATTAAGAAGACAGATGGCAAAT
GGTTATTTCTTAGAAGGTTTTGTACGTTTTAAAGAAGCCAAGGATAGTAATCAGGAGTTAATGAGTAT
45 TCCTTTTGTAGGATTTAATGGTGATTTTGCGAACCTACAAGCACTTGAAACACCGATTTATAAGACGC
TTTCTAAAGGTAGTTTCTACTATAAACCAAATGATACAACCTATAAAGACCAATTGGAGTACAATGAA
TCAGCTCCTTTTGAAAGCAACAACCTATACTGCCTTGTTAACACAATCAGCGTCTTGGGGCTATGTTGA
TTATGTCAAAAATGGTGGGGAGTTAGAATTAGCACCAGAGAGTCCAAAAAGAATTATTTTAGGAACTT
TTGAGAATAAGGTTGAGGATAAACAATTCATCTTTTGGAAAGAGATGCAGCGAATAATCCATATTTT
50 GCCATTTCTCAAATAAAGATGGAAATAGGGACGAAATCACTCCCCAGGCAACTTTCTTAAGAAATGT
TAAGGATATTTCTGCTCAAGTTCTAGATCAAAATGGAAATGTTATTTGGCAAAGTAAGGTTTTACCAT

CTTATCGTAAAAATTTCCATAATAATCCAAAGCAAAGTGATGGTCATTATCGTATGGATGCTCTTCAG
 TGGAGTGGTTTAGATAAGGATGGCAAAGTTGTAGCAGATGGTTTTTATACTTATCGCTTACGTTACAC
 ACCAGTAGCAGAAGGAGCAAATAGTCAGGAGTCAGACTTTTAAAGTACAAGTAAGTACTAAGTCACCAA
 ATCTTCCTTCACGAGCTCAGTTTGTATGAACTAATCGAACATTAAGCTTAGCCATGCCTAAGGAAAGT
 5 AGTTATGTTCTTACATATCGTTTACAATTAGTTTATCTCATGTTGTAAAAGATGAAGAATATGGGGA
 TGAGACTTCTTACCATTATTTCCATATAGATCAAGAAGGTAAAGTGACACTTCCTAAAAACGGTTAAGA
 TAGGAGAGAGTGAGGTTGCGGTAGACCCTAAGGCCTTGACACTTGTTGTGGAAGATAAAGCTGGTAAT
 TTCGCAACGGTAAAAATTGTCTGATCTCTTGAATAAGGCAGTAGTATCAGAGAAAGAAAACGCTATAGT
 AATTTCTAACAGTTTCAAATATTTTGATAACTTGAAAAAAGAACCTATGTTTATTTCTAAAAAAGAAA
 10 AAGTAGTAAACAAGAATCTAGAAGAAATAATATTAGTTAAGCCGCAAACCTACAGTTACTACTCAATCA
 TTGTCTAAA GAAATAACTAAATCAGGAAATGAGAAAGTCCTCACTTCTACAAACAATAATAGTAGCAG
 AGTAGCTAAGATCATATCACCTAAACATAACGGGGATTCTGTTAACCATAACCTTACCTAGTACATCAG
 ATAGAGCAACGAATGGTCTATTTGTTGGTACTTTGGCATTGTTATCTAGTTTACTTCTTTATTTGAAA
 CCCAAAAAGACTAAAAATAATAGTAAA

SEQ ID NO. 69

VDKHHSKKAILKLTLITTSILLMHSNQVNAEEQELKNQEQSPVIANVAQQPSPSVTTNTVEKTSVTAA
 SASNTAKEMGDTSVKNDKTEDELLEELSKNLDTSNLGADLEEEYPSKPETTNNKESNVVTNASTAIAQ
 20 KVPSAYEEVKPESKSSLAVLDTSKITKLQAITQRGKGNVVAIIDTGFDINHDI FRLDSPKDDKHSFKT
 KTEFEELKAKHNITYGKWVNDKIVFAHNYANNNTETVADIAAMKDGYGSEAKNISHGTHVAGIFVGNS
 KRPAINGLLLEGAAPNAQVLLMRI PDKIDSDFGEAYAKAITDAVNLGAKTINMSIGKTADSLIALND
 KVKLALKLASEKGVAVVVAAGNEGAFGMDYSKPLSTNPDYGTVNSPAISEDTL SVASYESLKTISEVV
 ETTIEGKLVKLPIVTSKPFDDKGKAYDVVYANYGAKKDFEGKDFKGKIALIERGGGLDFMTKI THATNA
 GVVGIVIFNDQEKRGNF LIPYRELPGIISKVDGERIKNTSSQLTFNQSFVVDSQGGNRMLEQSSWG
 25 VTAEGAIPDVTASGFEIYSSTYNNQYQTM SGTSMASPHVAGLMTMLQSHLAEKYKGMNLD SKKLEL
 SKNILMSSATALYSEEDKAFYSPRQQGAGVVD AEKAIQAQYYITGNDGKAKINLKRMDKFDITVTIH
 KLVEGVKELYYQANVATEQVNKGKFALKPQALLDTNWQKVILRDKETQVRFTIDASQFSQKLKEQMAN
 GYFLEGFVR FKEAKDSNQELMSIPFVGFGNGDFANLQALETP IYKTL SKGSFYYPNDTTHKDQLEYNE
 SAPFESNNYTALLTQSASWGYVDYVKNNGGELELAPESPKRIILGT FENKVEDKTIHLLERDAANNPYF
 30 AISPNKDGNRDEITPQATFLRNVKDISAQVLDQNGNVIWQSKVLPSYRKNFHNPKQSDGHYRMDALQ
 WSGLDKDGKV VADGFYTYRLRYTPVAEGANSQESDFKVQVSTKSPNLPSRAQFDETNRTL SLAMPKES
 SYVPTYRLQLVL SHVVKDEEYGD ETSYHYFHDQEGKVTLPKTVKIGESEVA VDPKALT LVVEDKAGN
 FATVKLSDL LNKA VVSEKENAIVISNSFKYFDNLKKEPMFISKKEKVVNKNLEEIILVKPQTTVTTS
 35 LSKEITKSGNEKVL TSTNNNSSRVAKIISPKNHGDSVNHTLPSTSDRATNGLFVGTLALLSSLLLYLK
PKKTKNNSK

GBS 147 contains an N-terminal leader or signal sequence region which is indicated by the
 underlined sequence at the beginning of SEQ ID NO 69 above. In one embodiment, one or more
 amino acids from the leader or signal sequence region of GBS 147 are removed. An example of such
 40 a GBS 147 fragment is set forth below as SEQ ID NO: 70.

SEQ ID NO: 70

EEQELKNQEQSPVIANVAQQPSPSVTTNTVEKTSVTAA SASNTAKEMGDTSVKNDKTEDELLEELSKN
 LDTSNLGADLEEEYPSKPETTNNKESNVVTNASTAIAQKVPSAYEEVKPESKSSLAVLDTSKITKLQA
 45 ITQRGKGNVVAIIDTGFDINHDI FRLDSPKDDKHSFKTKTEFEELKAKHNITYGKWVNDKIVFAHNYA
 NNTETVADIAAMKDGYGSEAKNISHGTHVAGIFVGNSKRPAINGLLLEGAAPNAQVLLMRI PDKIDS
 DKFGEAYAKAITDAVNLGAKTINMSIGKTADSLIALNDKVKLALKLASEKGVAVVVAAGNEGAFGMDY
 SKPLSTNPDYGTVNSPAISEDTL SVASYESLKTISEVVETTIEGKLVKLPIVTSKPFDDKGKAYDVVYA
 NYGAKKDFEGKDFKGKIALIERGGGLDFMTKI THATNAGVVGIVIFNDQEKRGNF LIPYRELPGIISK
 50 KVDGERIKNTSSQLTFNQSFVVDSQGGNRMLEQSSWGVTAEGAIPDVTASGFEIYSSTYNNQYQTM
 SGTSMASPHVAGLMTMLQSHLAEKYKGMNLD SKKLEL SKNILMSSATALYSEEDKAFYSPRQQGAGV

VDAEKAIQAQYYITGNDGKAKINLKRMDGKFDITVTIHKLVKELYYQANVATEQVNGKGFALKPQ
 ALLDTNWQKVILRDKETQVRFTIDASQFSQKLKEQMANGYFLEGFVRFEAKDSNQELMSIPFVGFGN
 DFANLQALETPIYKTLKSGSFYYKPNDDTHKDQLEYNESAPFESNNYTALLTQSASWGYVDYVKNNGE
 LELAPESPKRIILGTFENKVEDKTIHLLERDAANNPYFAISPNDGGRDEITPQATFLRNVKDISAQV
 5 LDQNGNVIWQSKVLPSYRKNFHNPKQSDGHYRMDALQWSGLDKDGKVVADGFYTYRLRYTPVAEGAN
 SQESDFKVQVSTKSPNLPSRAQFDETNRTLSLAMPKESYVPTYRLQLVLVSHVVKDEEYGDETSYYHYF
 HIDQEGKVTLPKTVKIGESEVAVDPKALTLLVEDKAGNFATVKLSDLLNKAVVSEKENAIVISNSFKY
 FDNLLKKEPMFISKKEKVVNKNLEEIIILVKPQTTVTTSLSKEITKSGNEKVLSTNNNSSRVAKIISP
 KHNGDSVNHTLPSTSDRATNGLFVGTLLALLSSLLLYLKPKKTKNNK

GBS 147 also contains a C-terminal transmembrane and/or cytoplasmic region which may be located within the underlined sequence near the end of SEQ ID NO: 69 above. In one embodiment, one or more amino acids from the transmembrane and/or cytoplasmic region are removed. An example of such a GBS 147 fragment is set forth below as SEQ ID NO: 71.

SEQ ID NO: 71

VDKHHSKKAILKLTLITTSILMHNSNQVNAEEQELKNQEQSPVIANVAQQPSPSVTTNTVEKTSVTAA
 SASNTAKEMGDTSVKNDKTEDELLEELSKNLDTSNLGADLEEEYPSKPETNNKESNVVTNASTAIAQ
 KVPSAYEEVKPESKSSSLAVLDTSKITKLQAITQRGKGNVVAIIDTGFDINHDI FRLDSPKDDKHSFKT
 20 KTEFEELKAKHNITYGKWVNDKIVFAHNYANNNTETVADIAAAMKDGYGSEAKNISHGTHVAGIFVGNS
 KRPAINGLLLEGAAPNAQVLLMRI PDKIDSKDFGEAYAKAITDAVNLGAKTINMSIGKTADSLIALND
 KVKLALKLASEKGVAVVVAAGNEGAFGMDYSKPLSTNPDYGTVNSPAISEDTLVSVASYESLKTISEVV
 ETTIEGKLVKLPVITSKPFDKGKAYDVVYANYGAKKDFEGKDFKGKIALIERGGGLDFMTKI THATNA
 GVVGIVIFNDQEKRGNFILPYRELPGIISKVDGERIKNTSSQLTFNQSFVVDSQGGNRMLEQSSWG
 25 VTAEGA IKPDVTASGFEIYSSTYNNQYQTMSTMASPHVAGLMTMLQSHLAEKYKGMNLD SKKLLEL
 SKNILMSSATALYSEEDKAFYSPRQQGAGVDAEKAIQAQYYITGNDGKAKINLKRMDGKFDITVTIHK
 KLVKELYYQANVATEQVNGKGFALKPQALLDTNWQKVILRDKETQVRFTIDASQFSQKLKEQMAN
 GYFLEGFVRFEAKDSNQELMSIPFVGFGNDFANLQALETPIYKTLKSGSFYYKPNDDTHKDQLEYNE
 SAPFESNNYTALLTQSASWGYVDYVKNNGGELELAPESPKRIILGTFENKVEDKTIHLLERDAANNPYF
 30 AISPNKDGRDEITPQATFLRNVKDISAQVLDQNGNVIWQSKVLPSYRKNFHNPKQSDGHYRMDALQ
 WSGLDKDGKVVADGFYTYRLRYTPVAEGANSQESDFKVQVSTKSPNLPSRAQFDETNRTLSLAMPKES
 SYVPTYRLQLVLVSHVVKDEEYGDETSYYHYFHIDQEGKVTLPKTVKIGESEVAVDPKALTLLVEDKAGN
 FATVKLSDLLNKAVVSEKENAIVISNSFKYFDNLLKKEPMFISKKEKVVNKNLEEIIILVKPQTTVTTS
 LSKEITKSGNEKVLSTNNNSSRVAKIISP KHNGDSVNHT

In one embodiment, one or more amino acids from the leader or signal sequence region and one or more amino acids from the transmembrane or cytoplasmic region are removed from the GBS 147 sequence. An example of such a GBS 147 fragment is set forth below as SEQ ID NO 72.

SEQ ID NO: 72

EEQELKNQEQSPVIANVAQQPSPSVTTNTVEKTSVTAA SASNTAKEMGDTSVKNDKTEDELLEELSKN
 LDTSNLGADLEEEYPSKPETNNKESNVVTNASTAIAQKVPSAYEEVKPESKSSSLAVLDTSKITKLQAI
 ITQRGKGNVVAIIDTGFDINHDI FRLDSPKDDKHSFKTKTEFEELKAKHNITYGKWVNDKIVFAHNYA
 45 NNTETVADIAAAMKDGYGSEAKNISHGTHVAGIFVGNSKRPAINGLLLEGAAPNAQVLLMRI PDKIDS
 DKFGEAYAKAITDAVNLGAKTINMSIGKTADSLIALNDKVKLALKLASEKGVAVVVAAGNEGAFGMDY
 SKPLSTNPDYGTVNSPAISEDTLVSVASYESLKTISEVVETTIEGKLVKLPVITSKPFDKGKAYDVVYA
 NYGAKKDFEGKDFKGKIALIERGGGLDFMTKI THATNAGVVGIVIFNDQEKRGNFILPYRELPGIISK
 KVDGERIKNTSSQLTFNQSFVVDSQGGNRMLEQSSWGVTAEGA IKPDVTASGFEIYSSTYNNQYQTM
 SGTSMASPHVAGLMTMLQSHLAEKYKGMNLD SKKLLELSKNILMSSATALYSEEDKAFYSPRQQGAGV

VDAEKAI QAQYYITGNDGKAKINLKRMDKFDITVTIHKLVKEGVKELYYQANVATEQVNKGKFALKPQ
 ALLDTNWQKVILRDKETQVRFTIDASQFSQKLKEQMANGYFLEGFVRFEAKDSNQELMSIPFVGFNG
 DFANLQALETPITYKTLKSGSFYYKPNDTTHKDQLEYNESAPFESNNYTALLTQSASWGYVDYVKNNGGE
 LELAPES PKRIILGT FENKVEDKTIHLLERDAANNPYFAISPNDGNRDEITPQATFLRNVKDISAQV
 5 LDQNGNV IWQSKVLPSYRKNFHNPNKQSDGHYRMDALQWSGLDKDGKVVADGFYTYRLRYTPVAEGAN
 SQESDFKVQVSTKSPNLPSRAQFDETNRTL SLAMPKESSYVPTYRLQLVL SHVVKDEEYGD ETSYHYF
 HIDQEGKVTL PKTVKIGESEVA VDPKAL TLVVEDKAGNFATVKLSDLLNKAVVSEKENAIVISNSFKY
 FDNLKKE PMFISKKEKVVNKNLEEI ILVKPQTTVTTQSLSKETKSGNEKVL TSTNNNSSRVAKIISP
 KHNGDSVNHT

GBS 173

GBS 173 refers to an amidase family protein. Nucleotide and amino acid sequences of GBS
 173 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 8787 and
 SEQ ID 8788. These sequences are set forth below as SEQ ID NOS 73 and 74:

SEQ ID NO. 73

ATGAAACGTAAATACTTTATTCTTAATACGGTGACGGTTTTTAACGTTAGCTGCTGCAATGAATACTAG
 CAGTATCTATGCTAATAGTACTGAGACAAGTGCTTCAGTAGTTCCTACTACAAATACTATCGTTCAAA
 CTAATGACAGTAATCCTACCGCAAAATTTGTATCAGAATCAGGACAATCTGTAATAGGTCAAGTAAAA
 20 CCAGATAATTCTGCGGCGCTTACAACAGTTGACACGCCTCATCATATTTTCAGCTCCAGATGCTTTAAA
 AACAACTCAATCAAGTCCTGTGCTTGAGAGTACTTCTACTAAGTTAACTGAAGAGACTTACAACAAA
 AAGATGGTCAAGATTTAGCCAACATGGTGAGAAGTGGTCAAGTTACTAGTGAGGAACCTGTTAATATG
 GCATACGATATTTATTGCTAAAGAAAACCCATCTTTAAATGCAGTCATTACTACTAGACGCCAAGAAGC
 TATTGAAGAGGCTAGAAAACCTTAAAGATACCAATCAGCCGTTTTTAGGTGTTCCCTTGTTAGTCAAGG
 25 GGTTAGGGCACAGTATTAAAGGTGGTGAAACCAATAATGGCTTGATCTATGCAGATGGAAAAATTAGC
 ACATTTGACAGTAGCTATGTCAAAAAATATAAAGATTTAGGATTTATTATTTTAGGACAAACGAACTT
 TCCAGAGTATGGGTGGCGTAATATAACAGATTCTAAATTATACGGTCTAACGCATAATCCTTGCGATC
 TTGCTCATAATGCTGGTGGCTCTTCTGGTGGAAGTGCAGCAGCCATTGCTAGCGGAATGACGCCAATT
 GCTAGCGGTAGTGATGCTGGTGGTCTATCCGTATTCCATCTTCTTGGACGGGCTTGGTAGGTTTAAA
 30 ACCAACAAGAGGATTGGTGAGTAATGAAAAGCCAGATTCGTATAGTACAGCAGTTCATTTCCATTAA
 CTAAGTCATCTAGAGACGCAGAAACATTATTAACCTTATCTAAAGAAAAGCGATCAAACGCTAGTATCA
 GTTAATGATTTAAAATCTTTACCAATTGCTTATACTTTGAAATCACCAATGGGAACAGAAGTTAGTCA
 AGATGCTAAAAACGCTATTATGGACAACGTCACATTCTTAAGAAAACAAGGATTCAAAGTAACAGAGA
 TAGACTTACCAATTGATGGTAGAGCATTAAATGCGTGATTATTCAACCTTGGCTATTGGCATGGGAGGA
 35 GCTTTTTCAACAATTGAAAAAGACTTAAAAAACATGGTTTTTACTAAAGAAGACGTTGATCCTATTAC
 TTGGGCAGTTTCATGTTATTTATCAAAATTGAGATAAGGCTGAACTTAAGAAATCTATTATGGAAGCCC
 AAAACATATGGATGATTATCGTAAGGCAATGGAGAAGCTTCACAAGCAATTTCTTATTTTCTTATCG
 CCAACGACCGCAAGTTTAGCCCTCTAAATACAGATCCATATGTAACAGAGGAAGATAAAAGAGCGAT
 TTATAATATGGAAAACCTTGAGCCAAAGAAGAAAGATTGCTCTCTTTAATCGCCAGTGGGAGCCTATGT
 40 TGCGTAGAACACCTTTTACACAAATTGCTAATATGACAGGACTCCCAGCTATCAGTATCCCGACTTAC
 TTATCTGAGTCTGGTTTACCCATAGGGACGATGTTAATGGCAGGTGCAAACCTATGATATGGTATTAAT
 TAAATTTGCAACTTTCTTTGAAAAACATCATGGTTTTAATGTTAAATGGCAAAGAATAATAGATAAAG
 AAGTGAAACCATCTACTGGCCTAATACAGCCTACTAACTCCCTCTTTAAAGCTCATTCATCATTAGTA
 AATTTAGAAAGAAAATTCACAAGTTACTCAAGTATCTATCTTAAAAATGGATGAAATCGTCTGTTAA
 45 AAATAAACCATCCGTAATGGCATATCAAAAAGCACTTCCTAAAACAGGTGATACAGAATCAAGCCTAT
 CTCAGTTTTAGTAGTAACCCTTTTATTAGCTTGTTTTAGCTTTGTAACAAAAAGAATCAGAAAAGT

SEQ ID NO. 74

MKRKYFI LNTVTVLTLAAAMNTSSIIYANSTETSASVVPTTNTIVQTNDSNPTAKFVSESGQSVIGQVK
 PDNSAALT TVDTPHHISAPDALKTTQSSPVVESTSTKLTEETYKQKDGQDLANMVRSGQVTSEELVNM
 5 AYDIIAKENPSLNAVITTRRQEAIEEARKLKDTNQPFLLVGLKGLGHSIKGGETNNGLIYADGKIS
 TFDSSYVKKYKDLGFII LGQTNFPEYGWRNITDSKLYGLTHNPWDLAHNAGGSSGGSAAAIASGMTPI
 ASGSDAGGSIRIPSSWTGLVGLKPTRGLVSNKPDSTAVHFPLTKSSRDAETLLTYLKSDQTLVS
 VNDLKSLPIAYTLKSPMGTEVSQDAKNAIMDNVTFLRKQGFVTEIDLPIDGRALMRDYSTLAIGMGG
 10 AFSTIEKDLKKHGFTKEDVDPI TWAVHVIYQNSDKAELKKSIMEAQKHMDYRKAMEKLHKQFPFI
 PTTASLAPLNTDPYVTEEDKRAIYNMENLSQEERIALFNRQWEPMLRRTPTFTQIANMTGLPAISIPTY
 LSEGLPIGTMLMAGANYDMVLIKFATFFEKHHGFNVKWQRIIDKEVKPSTGLIQPTNSLFKAHSSLV
 NLEENSQVTQVSISKKWMKSSVKNKPSVMAYQKALPKTGTESSLS PVLVVTLLLACFSFVTKKNQKS

GBS 173 contains an N-terminal leader or signal sequence region which is indicated by the
 15 underlined sequences at the beginning of SEQ ID NO: 74 above. In one embodiment, one or more
 amino acids from the leader or signal sequence of GBS 173 are removed. An example of such a GBS
 173 fragment is set forth below as SEQ ID NO: 75.

SEQ ID NO: 75

TTNTIVQTNDSNPTAKFVSESGQSVIGQVKPDNSAALT TVDTPHHISAPDALKTTQSSPVVESTSTKL
 20 TEETYKQKDGQDLANMVRSGQVTSEELVNMAYDIIAKENPSLNAVITTRRQEAIEEARKLKDTNQPFLL
 GVPLLVKGLGHSIKGGETNNGLIYADGKISTFDSSYVKKYKDLGFII LGQTNFPEYGWRNITDSKLYG
 LTHNPWDLAHNAGGSSGGSAAAIASGMTPIASGSDAGGSIRIPSSWTGLVGLKPTRGLVSNKPDSTAV
 25 TAVHFPLTKSSRDAETLLTYLKSDQTLVSVNDLKSLPIAYTLKSPMGTEVSQDAKNAIMDNVTFLRK
 QGFVTEIDLPIDGRALMRDYSTLAIGMGGAFSTIEKDLKKHGFTKEDVDPI TWAVHVIYQNSDKAEL
 KKSIMEAQKHMDYRKAMEKLHKQFPFI PTTASLAPLNTDPYVTEEDKRAIYNMENLSQEERIALF
 NRQWEPMLRRTPTFTQIANMTGLPAISIPTYLSEGLPIGTMLMAGANYDMVLIKFATFFEKHHGFNVK
 30 WQRIIDKEVKPSTGLIQPTNSLFKAHSSLVNLEENSQVTQVSISKKWMKSSVKNKPSVMAYQKALPKT
 GTESSLS PVLVVTLLLACFSFVTKKNQKS

GBS 173 may also contain a C-terminal transmembrane and/or cytoplasmic region which
 may be located within the underlined region near the end of SEQ ID NO: 74 above. In one
 embodiment, one or more amino acids from the transmembrane or cytoplasmic region of GBS 173 are
 removed. An example of such a GBS 173 fragment is set forth below as SEQ ID NO: 76.

SEQ ID NO: 76

MKRKYFI LNTVTVLTLAAAMNTSSIIYANSTETSASVVPTTNTIVQTNDSNPTAKFVSESGQSVIGQVK
 PDNSAALT TVDTPHHISAPDALKTTQSSPVVESTSTKLTEETYKQKDGQDLANMVRSGQVTSEELVNM
 40 AYDIIAKENPSLNAVITTRRQEAIEEARKLKDTNQPFLLVGLKGLGHSIKGGETNNGLIYADGKIS
 TFDSSYVKKYKDLGFII LGQTNFPEYGWRNITDSKLYGLTHNPWDLAHNAGGSSGGSAAAIASGMTPI
 ASGSDAGGSIRIPSSWTGLVGLKPTRGLVSNKPDSTAVHFPLTKSSRDAETLLTYLKSDQTLVS
 VNDLKSLPIAYTLKSPMGTEVSQDAKNAIMDNVTFLRKQGFVTEIDLPIDGRALMRDYSTLAIGMGG
 AFSTIEKDLKKHGFTKEDVDPI TWAVHVIYQNSDKAELKKSIMEAQKHMDYRKAMEKLHKQFPFI
 45 PTTASLAPLNTDPYVTEEDKRAIYNMENLSQEERIALFNRQWEPMLRRTPTFTQIANMTGLPAISIPTY
 LSEGLPIGTMLMAGANYDMVLIKFATFFEKHHGFNVKWQRIIDKEVKPSTGLIQPTNSLFKAHSSLV
 NLEENSQVTQVSISKKWMKSSVKNK

In one embodiment, one or more amino acids from the leader or signal sequence region and one or more amino acids from the transmembrane or cytoplasmic region are removed. An example of such a GBS 173 fragment is set forth below as SEQ ID NO: 77.

5 **SEQ ID NO: 77**

TTNTIVQTNDNPTAKFVSESGQSVIGQVKPDNSAALTTVDTPHHISAPDALKTTQSSPVVESTSTKL
TEETYKQKDGQDLANMVRSGQVTSEELVNMAYDIIAKENPSLNAVITTRRQEAIEEARKLKDTNQPFLL
GVPLLVKGLGHSIKGGETNNGLIYADGKISTFDSSYVKKYKDLGFIILGQTNFPFYGWRNITDSKLYG
LTHNPWDLAHNAGGSSGGSAASGMPPIASGSDAGGSIRIPSSWTGLVGLKPTRGLVSNKPDSSYS
10 TAVHFPLTKSSRDAETLLTYLKKSQDTLVSVNDLKSPLIAYTLKSPMGTEVSQDAKNAIMDNVTFRLK
QGFKVTEIDLPIDGRALMRDYSTLAIGMGAFSTIEKDLKKHGFTEKEDVDPIWAVHVIYQNSDKAEL
KKSIMEAQKHMDDYRKAMEKLHKQFPIFLSPTTASLAPLNTDPYVTEEDKRAIYNMENLSQEERIALF
NRQWEPMLRRTPTFTQIANMTGLPAISIPTYLSESGLPITGMLMAGANYDMVLIKFFATFFEKHHGFNVK
15 WQRIIDKEVKPSTGLIQPTNSLFAHSSLVNLEENSQVTQVSISKKWMKSSVKNK

15 **GBS 313**

Nucleotide and amino acid sequences of GBS 313 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 4089 and SEQ ID 4090. These sequences are set forth as SEQ ID NOS 78 and 79 below:

20 **SEQ ID NO. 78**

ATGAAACGTATTGCTGTTTTAACTAGTGGTGGTGACGCCCTGGTATGAACGCTGCTATCCGTGCAGT
TGTTCTGTAAGCAATTTCTGAAGGTATGGAAGTTTACGGCATCAACCAAGGTTACTATGCTATGGTGA
CAGGGGATATTTTCCCTTTGGATGCTAATTCTGTTGGGGATACTATCAACCGTGGAGGAACGTTTTTA
25 CGTTCAGCACGTTATCCTGAATTTGCTGAACTTGAAGGTCAGCTTAAAGGGATTGAACAGCTTAAAAA
ACACGGTATTGAAGGTGTAGTAGTTATCGGTGGTGATGGTTCTTATCATGGTGCTATGCGTCTAACTG
AGCACGGTTTCCAGCTGTTGGTTTGCCGGGTACAATTGATAACGATATCGTTGGCACTGACTATACT
ATTGGTTTTTGACACAGCAGTTGCGACAGCAGTTGAGAATCTTGACCGTCTTCGTGATACATCAGCAAG
TCATAACCGTACTTTTTGTTGTTGAGGTTATGGGAAGAAATGCAGGAGATATCGCTCTTTGGTCAGGTA
30 TCGCTGCAGGTGCAGATCAAATTATTGTTCTGGAAGAAGAGTTCAATATTGATGAAGTTGTCTCAAT
GTTAGAGCTGGCTATGCAGCTGGTAAACATCACCAAATCATCGTCTTGCAGAAGGTGTTATGAGTGG
TGATGAGTTTGCAGGAAACAATGAAAGCAGCAGGAGACGATAGCGATCTTCGTGTGACGAATTTAGGAC
ATCTGCTCCGTGGTGGTAGTCCGACGGCTCGTGATCGTGTCTTAGCATCTCGTATGGGAGCGTACGCT
GTTCAATTGTTGAAAGAAGGTCTGTTGGTTTAGCCGTTGGTGTCCACAACGAAGAAATGGTTGAAAG
35 TCCAATTTTAGGTTTAGCAGAAGAAGGTGCTTTGTTTCTGCTTACTGATGAAGGAAAAATCGTTGTTA
ATAATCCGCATAAAGCGGACCTTCGCTTGGCAGCACTTAATCGTGACCTTGCCAACCAAGTAGTAA

SEQ ID NO. 79

MKRIAVLTSGGDAPGMNAAIRAVVRKAISEGMEVYGINQGYGMYTGDIFPLDANSVGDITINRGGTFL
40 RSARYPEFAELEGQLKGIEQLKKHGIQGVVIGGDSYHGAMRLTEHGFPVAVGLPGTIDNDIVGTDYT
IGFDTAVATAVENLDRLRDTASASHNRTFVVEVMGRNAGDIALWSGIAAGADQIIVPEEEFNIDEVVS
VRAGYAAGKHHQIIVLAEGVMSGDEFKTMKAAGDSDLRVTNLGHLLRGGSPARTDRVLASRMGAYA
VQLLKEGRGGLAVGVHNEEMVESPIGLAEAGALFSLTDEGKIVVNNPHKADLRLAALNRDLANQSSK

GBS 328

GBS 328 belongs to the 5'-nucleotidase family. Nucleotide and amino acid sequences of GBS 328 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 6015 and SEQ ID 6016. These sequences are set forth below as SEQ ID NOS 80 and 81:

SEQ ID NO. 80

ATGAAAAAGAAATTATTTTGAAAAGTAGTGTTCTTGGTTTAGTCGCTGGGACTTCTATTATGTTCTC
 AAGCGTGTTTCGCGGACCAAGTCGGTGTCCAAGTTATAGGCGTCAATGACTTTCATGGTGCACCTTGACA
 10 ATACTGGAACAGCAAATATGCCTGATGGAAAAGTTGCTAATGCTGGTACTGCTGCTCAATTAGATGCT
 TATATGGATGACGCTCAAAAAGATTTCAAACAACTAACCCTAATGGTGAAAGCATTAGGGTTCAAGC
 AGGCGATATGGTTGGAGCAAGTCCAGCCAACTCTGGGCTTCTTCAAGATGAACCAACTGTCAAAAATT
 TTAATGCAATGAATGTTGAGTATGGCACATTGGGTAACCATGAATTTGATGAAGGGTTGGCAGAATAT
 AATCGTATCGTTACTGGTAAAGCCCCTGCTCCAGATTCTAATATTAATAATATTACGAAATCATACCC
 15 ACATGAAGCTGCAAAACAAGAAATTGTAGTGGCAAATGTTATTGATAAAGTTAACAACAAATTCCTT
 ACAATTGGAAGCCTTACGCTATTAAAAATATTCCTGTAAATAACAAAAGTGTGAACGTTGGCTTTATC
 GGGATTGTCACCAAAGACATCCCAAACCTTGTCTTACGTAAAAATTTATGAACAATATGAATTTTTAGA
 TGAAGCTGAAACAATCGTTAAATACGCCAAAGAATTACAAGCTAAAAATGTCAAAGCTATTGTAGTTC
 TCGCACATGTACCTGCAACAAGTAAAAATGATATTGCTGAAGGTGAAGCAGCAGAAATGATGAAAAAA
 20 GTC AATCAACTCTTCCCTGAAAATAGCGTAGATATTGCTCTTGTGCTGGACACAATCATCAATATACAAA
 TGGTCTTGTTGTTAAACTCGTATTGTACAAGCGCTCTCTCAAGGAAAAGCCTATGCTGATGTACGTG
 GTGTCTTAGATACTGATACACAAGATTTCAATTGAGACCCCTTCAGCTAAAGTAATTGCAGTTGCTCCT
 GGTAACAGCTAAAGTAAATGGTACTGCCGATATTCAGGCCATTGTTGACCAAGCTAATACTATCGTTAAACAAGT
 AACAGAAGCTAAAATTTGGTACTGCCGAGGTAAAGTGTGATGATTACGCGTTCTGTTGATCAAGATAATG
 25 TTAGTCCGGTAGGCAGCCTCATCAAGAGGCTCAACTAGCAATTGCTCGAAAAAGCTGGCCAGATATC
 GATTTTGGCCATGACAAATAATGGTGGCATTCTGCTGACTTACTCATCAAACCAGATGGAACAATCAC
 CTGGGGAGCTGCACAAGCAGTTCAACCTTTTGGTAATATCTTACAAGTCGTCGAAATTAGTGGTAGAG
 ATCTTTTATAAAGCACTCAACGAACAATACGACCAAAAAACAAAATTTCTTCTTCAAATAGCTGGTCTG
 CGATACACTTACACAGATAATAAAGAGGGCGGGGAAGAAACACCATTTAAAGTTGTAAAAGCTTATAA
 30 ATCAAATGGTGAGGAAATCAATCCTGATGCAAAATACAAATTAGTTATCAATGACTTTTTTATTCGGTG
 GTGGTGATGGCTTTGCAAGCTTCAGAAATGCCAACTTCTAGGAGCCATTAACCCCGATACAGAGGTA
 TTTATGGCCTATATCACTGATTTAGAAAAAGCTGGTAAAAAAGTGAGCGTTCCAAATAATAAACCTAA
 AATCTATGTCACCTATGAAGATGGTTAATGAACTATTACACAAAATGATGGTACACATAGCATTATTA
 AGAACTTTATTTAGATCGACAAGGAAATATTGTAGCACAAAGAGATTGTATCAGACACTTTAAACCAA
 35 ACAAATCAAATCTACAAAATCAACCCTGTAACCTACAATTACAAAAACAATTACACCAATTTAC
 AGCTATTAACCCTATGAGAAATTATGGCAAACCATCAAACCTCCACTACTGTAAAATCAAACAATTAC
 CAAAAACAACCTCTGAATATGGACAATCATTCCTTATGTCTGTCTTTGGTGTGACTTATAGGAATT
 GCTTTAAATACAAAGAAAAAACATATGAAA

SEQ ID NO. 81

MKKKIILKSSVLGLVAGTSIMFSSVFADQVGVQVIGVND~~FH~~GALDNTGTANMPDGKVANAGTAAQLDA
 YMDDAQKDFKQTNPNGESIRVQAGDMVGAS~~PAN~~SGLLQDEPTVKNFNAMNVEYGT~~LN~~HEFDEGLAEY
 NRIVTGKAPAPDSNINNITKSY~~PHE~~AAKQEI~~VVAN~~VIDKVNKQIPYNWKPYAIKNI~~PVNN~~KSVNVGFI
 GIVTKDIPNLVLRKNYEQYEF~~LDE~~AETIVKYAKELQAKNVKAI~~VVL~~AHVPATSKNDIAEGEAAEMMKK
 45 VNQLFPENSVDIVFAGHNH~~QY~~TNGLVGKTRIVQALSQ~~GK~~AYADVRGVLD~~TD~~TQDFIETPSAKVIAVAP
 GKKTGSADIQAI~~VD~~QANTIVKQVTEAKIGTAEVSVMITRSVDQDNVSPVGS~~LITE~~AQLAIARKSWPDI
 DFAMTNNGGIRADLLIKPDG~~IT~~WGAAQAVQPF~~GNIL~~QVVEITGRDLYKALNEQYDQKQ~~NFF~~LQIAGL
 RYTYTDNKEGGEETPFKVVKAYKSN~~GEE~~INPD~~AKY~~KLVIN~~DF~~LFGG~~GD~~GFASF~~RNA~~KL~~LGA~~INPDTEV
 FMAYITDLEKAGKKVSV~~PNN~~KPKIYVTM~~KMV~~NETITQNDGTHSIIKKLYLDRQGNIVAQEIVSD~~T~~LNQ
 50 TSKSKSTKINPVTTIHKKQLHQFTAINPMRNYGKPSNSTTVKSKQLPKTNSEY~~Q~~SFLMSVFGVGLIGI
 ALNTKKKHKMK

GBS 328 may contain an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO: 81 above. In one embodiment, one or more amino acids from the leader or signal sequence region of GBS 328 are removed. An example of such a GBS 328 fragment is set forth below as SEQ ID NO: 82.

SEQ ID NO: 82

HGALDNTGTANMPDGKVANAGTAAQLDAYMDDAQKDFKQTNPNGESIRVQAGDMVGASPANSGLLQDE
PTVKNFNAMNVEYGTGLGNHEFDEGLAEYNRIVTGKAPAPDSNINNITKSY PHEAAKQEIVVANVIDKV
NKQIPYNWKPYAIKNIPVNNKSVNVGFIGIVTKDIPNLVLRKNYEQYEF LDEAETIVKYAKELQAKNV
KAI VVLAHV PATSKNDIAEGEAAEMMKVNQLFPENSVDIVFAGHNHQYTNGLVGKTRIVQALSQGKA
YADV RGVLD TDTQDFIETPSAKVIAVAPGKKTGSADIQAIVDQANTIVKQVTEAKIGTAEVSVMITRS
VDQDNVSPVGS LITEAQLAIARKSWPDIDFAMTNNGGIRADLLIKPDGTITWGAAQAVQPF GNILQVV
EITGRDLYKALNEQYDQKQNF FLQIAGLRYTYTDNKEGGEETPFKVVKAYKSN GEEINPDAKYKLVIN
DFLFGGGDGFASFRNAKLLGAINPDTEVF MAYITDLEKAGKKVSV PNNKPKIYVTM KVMNETITQNDG
THSIIKKLYLDRQGNIVAQEIVSDTLNQTKSKSTKINPVTTIHKKQLHQFTAINPMRNYGKPSNSTTV
KSKQLPKTNSEYQSF LMSVFGVGLIGIALNTKKKHKMK

GBS 328 may also contain a transmembrane and/or cytoplasmic domain region. In one embodiment, one or more amino acids from the transmembrane and/or cytoplasmic domain region of GBS 328 are removed. An example of such a GBS 328 fragment is set forth below as SEQ ID NO: 83.

SEQ ID NO: 83

MKKKIIILKSSVLGLVAGTSIMFSSVFADQVG VQVIGVND F HGALDNTGTANMPDGKVANAGTAAQLDA
YMDDAQKDFKQTNPNGESIRVQAGDMVGASPANSGLLQDEPTVKNFNAMNVEYGTGLGNHEFDEGLAEY
NRIVTGKAPAPDSNINNITKSY PHEAAKQEIVVANVIDKVNKQIPYNWKPYAIKNIPVNNKSVNVGFI
GIVTKDIPNLVLRKNYEQYEF LDEAETIVKYAKELQAKNVKAI VVLAHV PATSKNDIAEGEAAEMMKK
VNQLFPENSVDIVFAGHNHQYTNGLVGKTRIVQALSQGKAYADV RGVLD TDTQDFIETPSAKVIAVAP
GKKTGSADIQAIVDQANTIVKQVTEAKIGTAEVSVMITRSVDQDNVSPVGS LITEAQLAIARKSWPDI
DFAMTNNGGIRADLLIKPDGTITWGAAQAVQPF GNILQVVEITGRDLYKALNEQYDQKQNF FLQIAGL
RYTYTDNKEGGEETPFKVVKAYKSN GEEINPDAKYKLVINDFLFGGGDGFASFRNAKLLGAINPDTEV
FMAYITDLEKAGKKVSV PNNKPKIYVTM KVMNETITQNDGTHSIIKKLYLDRQGNIVAQEIVSDTLNQ
TKSKSTKINPVTTIHKKQLHQFTAINPMRNYGKPSNSTTVKS

In one embodiment, one or more amino acids from the leader or signal sequence region and one or more amino acids from the transmembrane or cytoplasmic region of GBS 328 are removed. An example of such a GBS 328 fragment is set forth below as SEQ ID NO: 84.

SEQ ID NO: 84

HGALDNTGTANMPDGKVANAGTAAQLDAYMDDAQKDFKQTNPNGESIRVQAGDMVGASPANSGLLQDE
PTVKNFNAMNVEYGTGLGNHEFDEGLAEYNRIVTGKAPAPDSNINNITKSY PHEAAKQEIVVANVIDKV
NKQIPYNWKPYAIKNIPVNNKSVNVGFIGIVTKDIPNLVLRKNYEQYEF LDEAETIVKYAKELQAKNV
KAI VVLAHV PATSKNDIAEGEAAEMMKVNQLFPENSVDIVFAGHNHQYTNGLVGKTRIVQALSQGKA
YADV RGVLD TDTQDFIETPSAKVIAVAPGKKTGSADIQAIVDQANTIVKQVTEAKIGTAEVSVMITRS
VDQDNVSPVGS LITEAQLAIARKSWPDIDFAMTNNGGIRADLLIKPDGTITWGAAQAVQPF GNILQVV

EI TGRDLYKALNEQYDQKQNFLLQIAGLRYTYTDNKEGGEETPFKVVKAYKSNNGEEINPDACYKLVIN
DFLFGGGDGFASFRNAKLLGAINPDTEVFMAIITDLEKAGKKVSPNNPKIYVTMKNVNETITQNDG
THSIIKKLYLDRQGNIVAQEIVSDTLNQT KSKSTKINPVTTIHKKQLHQFTAINPMRNYGKPSNSTTV
KS

GBS 656

GBS 656 refers to a putative DNA-entry nuclease. Nucleotide and amino acid sequences of
GBS 656 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 9323
and SEQ ID 9324. These sequences are set forth below as SEQ ID NOS 85 and 86:

SEQ ID NO. 85

ATGAAAAGATTACATAAACTGTTTATAACCGTAATTGCTACATTAGGTATGTTGGGGGTAATGACCTT
TGGTCTTCCAACGCAGCCGCAAAACGTAACGCCGATAGTACATGCTGATGTCAATTCATCTGTTGATA
CGAGCCAGGAATTTCAAATAATTTAAAAAATGCTATTGGTAACCTACCATTTCAATATGTTAATGGT
ATTTATGAATTAAATAATAATCAGACAAATTTAAATGCTGATGTCAATGTTAAAGCGTATGTTCAAAA
TACAATTGACAATCAACAAAGACTATCAACTGCTAATGCAATGCTTGATAGAACCATTTCGTCAATATC
AAAATCGCAGAGATACCACTCTTCCCGATGCAAATTGGAAACCATTAGGTTGGCATCAAGTAGCTACT
AATGACCATTATGGACATGCAGTCGACAAGGGGCATTTAATTGCCTATGCTTTAGCTGGAAATTTCAA
AGGTTGGGATGCTTCCGTGTCAAATCCTCAAAATGTTGTACACAAACAGCTCATTTCCAACCAATCAA
ATCAAAAAATCAATCGTGGACAAAATTATTATGAAAGCTTAGTTGTAAGGCGGTTGACCAAAACAAA
CGTGTTTCGTTACCGTGTAACCTCCATTGTACCGTAATGATACTGATTAGTTCCATTTGCAATGCACCT
AGAAGCTAAATCACAAGATGGCACATTAGAATTTAATGTTGCTATTCCAAACACACAAGCATCATACA
CTATGGATTATGCAACAGGAGAAATAACACTAAAT

SEQ ID NO. 86

MKRLHKLFIITVIATLGLVMTFGLPTQPQNVTPIVHADVNSSVDTSQEFQNNLKNAINGLPFQYVNG
IYELNNNQTNLNADVNVKAYVQNTIDNQQRSTANAMLDRTIRQYQNRDITLDPANWKPLGWHQVAT
NDHYGHAVDKGHLIAYALAGNFKGWDASVSNPQNVVTQTAHSNQSNQKINRGQNYYESLVRKAVDQNK
RVRYRVTPLYRNDTDLVPPFAMHLEAKSQDGTLEFNVAIPNTQASYTMDYATGEITLN

GBS 67

The following offers examples of preferred GBS 67 fragments. Nucleotide and amino acid
sequence of GBS 67 sequences from serotype V isolated strain 2603 are set forth below as SEQ ID
NOS: 87 and 88.

SEQ ID NO: 87

ATGAGAAAATACCAAAAATTTTCTAAAATATTGACGTTAAGTCTTTTTTGTGTCGCAAATACCGCT
TAA TACCAATGTTTTAGGGGAAAGTACCGTACCGGAAAATGGTGCTAAAGGAAAGTTAGTTGTTAAAA
AGACAGATGACCAGAACAAACCACTTTCAAAGCTACCTTTGTTTTTAAAACTACTGCTCATCCAGAA
AGTAAAATAGAAAAAGTAACTGCTGAGCTAACAGGTGAAGCTACTTTTGATAATCTCATACCTGGAGA
TTA TACTTTATCAGAAGAAACAGCGCCCGAAGGTTATAAAAAGACTAACCAGACTTGGCAAGTTAAGG
TTGAGAGTAATGGAAAACTACGATACAAAATAGTGGTGATAAAAATTCCACAATTGGACAAAATCAG
GAA GAACTAGATAAGCAGTATCCCCCAGGAAATTTATGAAGATACAAAGGAATCTTATAAACTTGA
GCA TGTTAAAGGTTTCAATGGAAGTCAGAGGCAAAAGCAGTTAACCCATATTCAAGTGAAG
GTGAGCATATAAGAGAAATTCAGAGGGGAACATTATCTAAACGTATTTTCAAGAGTAGGTGATTTAGCT
CATAATAAATATAAAATTGAGTTAACTGTCAGTGGA AAAACCATAGTAAAACAGTGACAAAACAAAA
GCC GTTAGATGTTGTCTTCGTACTCGATAATTCTAACTCAATGAATAACGATGGCCCAAATTTTCAA
GGCATAATAAAGCCAAGAAAGCTGCCGAAGCTCTTGGGACCGCAGTAAAAGATATTTTAGGAGCAAAC

AGTGATAATAGGGTTGCATTAGTTACCTATGGTTCAGATATTTTTGATGGTAGGAGTGTAGATGTCGT
 AAAAGGATTTAAAGAAGATGATAAATATTATGGCCTTCAAACCTAAGTTCACAATTCAGACAGAGAATT
 ATAGTCATAAACAATTAACAAATAATGCTGAAGAGATTATAAAAAGGATTCCGACAGAAGCTCCTAAA
 GCTAAGTGGGGATCTACTACCAATGGATTAACCTCCAGAGCAACAAAAGGAGTACTATCTTAGTAAAGT
 5 AGGAGAAACATTTACTATGAAAGCCTTCATGGAGGCAGATGATATTTTGAGTCAAGTAAATCGAAATA
 GTCAAAAAATTATTGTTTCATGTAACCTGATGGTGTTCCTACGAGATCATATGCTATTAATAATTTTAAA
 CTGGGTGCATCATATGAAAGCCAATTTGAACAAATGAAAAAAATGGATATCTAAATAAAAAGTAATTT
 TCTACTTACTGATAAGCCCCGAGGATATAAAAAGGAAATGGGGAGAGTTACTTTTTGTTTTCCCTTAGATA
 GTTATCAAACACAGATAATCTCTGGAACTTACAAAACTTCATTATTTAGATTTAAATCTTAATTAC
 10 CCTAAAGGTACAATTTATCGAAATGGACCAGTGAAAGAACATGGAACACCAACCAAACTTTATATAAA
 TAGTTTAAACAGAAAAATTATGACATTTTTAATTTTGGTATCGATATATCTGGTTTTAGACAAGTTT
 ATAATGAGGAGTATAAGAAAAATCAAGATGGTACTTTTCAAAAATTGAAAGAGGAAGCTTTTAAACTT
 TCAGATGGAGAAATCACAGAACTAATGAGGTCGTTCTCTTCCAAACCTGAGTACTACACCCCTATCGT
 AACTTCAGCCGATACATCTAACAATGAAATTTTATCTAAAATTGAGCAACAATTTGAAACGATTTTAA
 15 CAAAAGAAAACTCAATTGTTAATGGAACCTATCGAAGATCCTATGGGTGATAAAATCAATTTACAGCTT
 GGTAATGGACAAACATTACAGCCAAGTGATTATACTTTACAGGGAAATGATGGAAGTGAATGAAGGA
 TGGTATTGCAACTGGTGGGCCTAATAATGATGGTGGAACTTAAAGGGGGTTAAATTAGAATACATCG
 GAAATAAACTCTATGTTAGAGGTTTGAATTTAGGAGAAGGTCAAAAAGTAACACTCACATATGATGTG
 AAAGTAGATGACAGTTTTATAAGTAACAAATTCATGACACTAATGGTAGAACAACATTGAATCCTAA
 20 GTCAGAGGATCCTAATACACTTAGAGATTTTCCAATCCCTAAAATTCGTGATGTGAGAGAATATCCTA
 CAATAACGATTAAAAACGAGAAGAAGTTAGGTGAAATTGAATTTATAAAAGTTGATAAAGATAATAAT
 AAGTTGCTTCTCAAAGGAGCTACGTTTGAACCTCAAGAATTTAATGAAGATTATAAACTTTATTTACC
 AATAAAAAATAATAATTCAAAAGTAGTGACGGGAGAAAACGGCAAAAATTTCTTACAAAGATTTGAAAG
 25 ATGGCAAATATCAGTTAATAGAAGCAGTTTCGCCGGAGGATTATCAAAAATTACTAATAAACCAATT
 TTAACCTTTGAAGTGGTTAAAGGATCGATAAAAAATATAATAGCTGTTAATAAACAGATTTCTGAATA
 TCATGAGGAAGGTGACAAGCATTTAATTACCAACACGCATATTCACCAAAGGAATTATTCCTATGA
 CAGGTGGGAAAGGAATTCTATCTTTCATTTTAAATAGGTGGAGCTATGATGTCTATTGCAGGTGGAATT
 TATATTTGAAAAGGTATAAGAAATCTAGTGATATGTCCATCAAAAAGAT
 30 **SEQ ID NO: 88**
 MRKYQKFSKILTLSLFCLSQIPLNTNVLGESTVPENGAKGKLVVKKTDQNKPLSKATFVLKTTAHPE
 SKIEKVTAELTGEATFDNLI PGDYTLSEETAPEGYKKTNQWQVKVESNGKTTIQNSGDKNSTIGQNO
 EELDKQYPPTGIYEDTKESYKLEHVKGSPNGKSEAKAVNPYSSEGEHIREIPEGTLSKRISEVGD
 35 HNKYKIELTVSGKTIVKPVDKQKPLDVVFLDNSNSMNNDGPNFQRHNKAKKAAEALGTAVKDILGAN
 SDNRVALVTYGSDFDGRSVDVVKGFKEDDKYYGLQTKFTIQTENYSHKQLTNNAEEI IKRIPT
 AKWGSTTNGLTPEQQKEYYLSKVGETFTMKAFMEADDILSQVNRNSQKIIVHVTGVPTRSYAINNFK
 LGASYESQFEQMKKNGYLNKSNFLLTDPEDIKNGESYFLFPLDSYQTQIISGNLQKLHYLDLNLNY
 PKGTIYRNGPVKEHGTPTKLYINSLKQKNYDIFNFGIDISGFRQVYN EYKKNQDGT FQKLKEEAFKL
 40 SDGEITELMRSFSSKPEYYTPIVTSADTSNNEILSKIQQQFETILT KENSIVNGTIEDPMGDKINLQL
 GNGQTLQPSDYTLQNDGSVMKDGIATGGPNNDGGILKGVKLEYIGNKLYVRGLNLGEGQKVTLTYDV
 KLDDSFISNKFYDTNGRITTLNPKSEDPNLTDRDFIPKIRDVREYPTITIKNEKKLGEIEFIKVDKDN
 KLLKLGATFELQEFNEDYKLYLPKNNNSKVVTGENGKISYKDLKDGKYQLIEAVSPEDYQKITNKPI
 45 LTFEVVKGSIKNIIAVNKQISEYHEEGDKHLITNTHIPPKGIIPMTGGKGILSFILIGGAMMSIAGGI
YIWKRYKKSSDMSIKKD

GBS 67 contains a C-terminus transmembrane region which is indicated by the underlined region closest to the C-terminus of SEQ ID NO: 88 above. In one embodiment, one or more amino acids from the transmembrane region is removed and or the amino acid is truncated before the transmembrane region. An example of such a GBS 67 fragment is set forth below as SEQ ID NO: 89.

SEQ ID NO: 89

MRKYQKFSKILTLSLFCLSQIPLNTNVLGESTVPENGAKGKLVVKKTTDDQNKPLSKATFVLKTTAHPE
 SKIEKVTAELTGEATFDNLI PGDYTLSEETAPEGYKKTNQTWQVKVESNGKTTIQNSGDKNSTIGQNO
 EELDKQYPPTGIYEDTKESYKLEHVKGSPNGKSEAKAVNPYSSEGEHIREI PEGTLSKRISSEVGDLA
 5 HNKYKIELTVSGKTIVKPVDKQKPLDVVFVLDNSNSMNDGPNFQRHNKAKKAAEALGTAVKDILGAN
 SDNRVALVTYGSDFDGRSVDVVKGFKEDDKYGLQTKFTIQTENYSHKQLTNNAEEIIKRIPTTEAPK
 AKWGSTTNGLTPEQQKEYYLSKVGETFTMKAFMEADDILSQVNRNSQKIIVHVTDGVPTRSYAINNFK
 LGASYESQFEQMKKNGYLNKSNFLLTDKPEDIKNGESYFLFPLDSYQTQIISGNLQKLHYLDLNLNY
 10 PKGTIYRNGPVKEHGTPTKLYINSLKQKNYDIFNFGIDISGFRQVYNEEYKKNQDGTFOKLKEEAFKL
 SDGEITELMRSFSSKPEYYTPIVTSADTSNNEILSKIQQQFETILTKENSIVNGTIEDPMGDKINLQL
 GNGQTLQPSDYTLQNDGSVMKDGIATGGPNNDGGILKGVKLEYIGNKLYVRGLNLGEGQKVTLTYDV
 KLDDSFISNKFYDTNGRCTLNPKSEDPNTLRDFPIPKIRDVREYPTITIKNEKKLGEIEFIKVDKDNN
 KLLLKGATFELQEFNEDYKLYLPIKNNNSKVVTGENGKISYKDLKDGKYQLIEAVSPEDYQKITNKPI
 15 LTFEVVKGSIKNI IAVNKQISEYHEEGDKHLITNTHIPPKGIIPMTGGKGILS

GBS 67 contains an amino acid motif indicative of a cell wall anchor (an LPXTG motif):

SEQ ID NO: 90 *IPMTG*. (shown in *italics* in SEQ ID NO: 88 above). In some recombinant host cell systems, it may be preferable to remove this motif to facilitate secretion of a recombinant GBS 67 protein from the host cell. Accordingly, in one preferred fragment of GBS 67 for use in the invention, the transmembrane and the cell wall anchor motif are removed from GBS 67. An example of such a GBS 67 fragment is set forth below as SEQ ID NO: 91.

SEQ ID NO: 91

MRKYQKFSKILTLSLFCLSQIPLNTNVLGESTVPENGAKGKLVVKKTTDDQNKPLSKATFVLKTTAHPE
 SKIEKVTAELTGEATFDNLI PGDYTLSEETAPEGYKKTNQTWQVKVESNGKTTIQNSGDKNSTIGQNO
 25 EELDKQYPPTGIYEDTKESYKLEHVKGSPNGKSEAKAVNPYSSEGEHIREI PEGTLSKRISSEVGDLA
 HNKYKIELTVSGKTIVKPVDKQKPLDVVFVLDNSNSMNDGPNFQRHNKAKKAAEALGTAVKDILGAN
 SDNRVALVTYGSDFDGRSVDVVKGFKEDDKYGLQTKFTIQTENYSHKQLTNNAEEIIKRIPTTEAPK
 AKWGSTTNGLTPEQQKEYYLSKVGETFTMKAFMEADDILSQVNRNSQKIIVHVTDGVPTRSYAINNFK
 30 LGASYESQFEQMKKNGYLNKSNFLLTDKPEDIKNGESYFLFPLDSYQTQIISGNLQKLHYLDLNLNY
 PKGTIYRNGPVKEHGTPTKLYINSLKQKNYDIFNFGIDISGFRQVYNEEYKKNQDGTFOKLKEEAFKL
 SDGEITELMRSFSSKPEYYTPIVTSADTSNNEILSKIQQQFETILTKENSIVNGTIEDPMGDKINLQL
 GNGQTLQPSDYTLQNDGSVMKDGIATGGPNNDGGILKGVKLEYIGNKLYVRGLNLGEGQKVTLTYDV
 KLDDSFISNKFYDTNGRCTLNPKSEDPNTLRDFPIPKIRDVREYPTITIKNEKKLGEIEFIKVDKDNN
 35 KLLLKGATFELQEFNEDYKLYLPIKNNNSKVVTGENGKISYKDLKDGKYQLIEAVSPEDYQKITNKPI
 LTFEVVKGSIKNI IAVNKQISEYHEEGDKHLITNTHIPPKGI

The compositions of the invention may also include combinations including one or more known GBS antigens in combination with GBS 80.

There is an upper limit to the number of GBS antigens which will be in the compositions of the invention. Preferably, the number of GBS antigens in a composition of the invention is less than 20, less than 19, less than 18, less than 17, less than 16, less than 15, less than 14, less than 13, less than 12, less than 11, less than 10, less than 9, less than 8, less than 7, less than 6, less than 5, less than 4, or less than 3. Still more preferably, the number of GBS antigens in a composition of the invention

is less than 6, less than 5, or less than 4. Still more preferably, the number of GBS antigens in a composition of the invention is 3.

The GBS antigens used in the invention are preferably isolated, i.e., separate and discrete, from the whole organism with which the molecule is found in nature or, when the polynucleotide or polypeptide is not found in nature, is sufficiently free of other biological macromolecules so that the polynucleotide or polypeptide can be used for its intended purpose.

Fusion Proteins

The GBS antigens used in the invention may be present in the composition as individual separate polypeptides, but it is preferred that at least two (*i.e.* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or 18) of the antigens are expressed as a single polypeptide chain (a “hybrid” or “fusion” polypeptide). Such fusion polypeptides offer two principal advantages: first, a polypeptide that may be unstable or poorly expressed on its own can be assisted by adding a suitable fusion partner that overcomes the problem; second, commercial manufacture is simplified as only one expression and purification need be employed in order to produce two polypeptides which are both antigenically useful.

The fusion polypeptide may comprise two or more polypeptide sequences from the group consisting of GBS 80, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690 and GBS 691. Preferably, the polypeptide sequences are selected from the group consisting of GBS 80, GBS 104 and GBS 322. Most preferably, the fusion peptide includes a polypeptide sequence from GBS 80. Accordingly, the invention includes a fusion peptide comprising a first amino acid sequence and a second amino acid sequence, wherein said first and second amino acid sequences are selected from a GBS antigen or a fragment thereof of the above antigen group. Preferably, the first and second amino acid sequences in the fusion polypeptide comprise different epitopes.

EXAMPLE 7: Examples of fragments for fusion proteins from GBS 80 with GBS 104, and GBS 322

Examples of GBS fragments for fusion proteins are provided from GBS 322, GBS 104, and GBS 80. One example of a fragment of GBS 322 in a fusion protein is a 407 amino acid fragment with the signal peptide removed. Fragments of GBS 104 may also be incorporated in fusion proteins. An example of GBS 104 fragments includes an 830 amino acid fragment, a 359 amino acid fragment from near the N-terminus, a 581 amino acid fragment from near the N-terminus, and a 740 amino acid fragment from near the N-terminus. Examples of GBS 80 fragments include a 446 amino acid fragment and a 235 amino acid fragment. Table 13 below summarizes the examples of fragments for fusion proteins and their locations within the corresponding full length GBS protein.

Table 13: Active Maternal Immunization Assay using combinations of GBS 80 with GBS 104 and GBS 322

GBS	Size (AA)	SEQ ID NO	From ... to
322	407	92	25-432
104	830	96	28-858
104 N1	359	97	28-387
104 N2	581	98	28-609
104 N3	740	99	28-768
80	446	100	37-483
80N	235	101	37-272

5

Hybrids (or fusions) consisting of amino acid sequences from two, three, four, five, six, seven, eight, nine, or ten GBS antigens are preferred. In particular, hybrids consisting of amino acid sequences from two, three, four, or five GBS antigens are preferred.

10 Different hybrid polypeptides may be mixed together in a single formulation. Within such combinations, a GBS antigen may be present in more than one hybrid polypeptide and/or as a non-hybrid polypeptide. It is preferred, however, that an antigen is present either as a hybrid or as a non-hybrid, but not as both.

Hybrid polypeptides can be represented by the formula $\text{NH}_2\text{-A-}\{-\text{X-L-}\}_n\text{-B-COOH}$, wherein:
 15 X is an amino acid sequence of a GBS antigen or a fragment thereof from the antigen group set forth above; L is an optional linker amino acid sequence; A is an optional N-terminal amino acid sequence; B is an optional C-terminal amino acid sequence; and n is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15.

If a -X- moiety has a leader peptide sequence in its wild-type form, this may be included or omitted in the hybrid protein. In some embodiments, the leader peptides will be deleted except for that of the -X- moiety located at the N-terminus of the hybrid protein *i.e.* the leader peptide of X_1 will
 20 be retained, but the leader peptides of $X_2 \dots X_n$ will be omitted. This is equivalent to deleting all leader peptides and using the leader peptide of X_1 as moiety -A-.

For each n instances of $\{-\text{X-L-}\}$, linker amino acid sequence -L- may be present or absent. For instance, when $n=2$ the hybrid may be $\text{NH}_2\text{-X}_1\text{-L}_1\text{-X}_2\text{-L}_2\text{-COOH}$, $\text{NH}_2\text{-X}_1\text{-X}_2\text{-COOH}$, $\text{NH}_2\text{-X}_1\text{-L}_1\text{-X}_2\text{-COOH}$, $\text{NH}_2\text{-X}_1\text{-X}_2\text{-L}_2\text{-COOH}$, *etc.* Linker amino acid sequence(s) -L- will typically
 25 be short (*e.g.* 20 or fewer amino acids *i.e.* 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1). Examples comprise short peptide sequences which facilitate cloning, poly-glycine linkers (*i.e.* comprising Gly_n where $n = 2, 3, 4, 5, 6, 7, 8, 9, 10$ or more), and histidine tags (*i.e.* His_n where $n = 3, 4, 5, 6, 7, 8, 9, 10$ or more). Other suitable linker amino acid sequences will be apparent to those skilled in the art. A useful linker is GSGGGG, with the Gly-Ser dipeptide being formed from a

*Bam*HI restriction site, thus aiding cloning and manipulation, and the (Gly)₄ tetrapeptide being a typical poly-glycine linker.

-A- is an optional N-terminal amino acid sequence. This will typically be short (*e.g.* 40 or fewer amino acids *i.e.* 39, 38, 37, 36, 35, 34, 33, 32, 31, 30, 29, 28, 27, 26, 25, 24, 23, 22, 21, 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1). Examples include leader sequences to direct protein trafficking, or short peptide sequences which facilitate cloning or purification (*e.g.* histidine tags *i.e.* His_{*n*}, where *n* = 3, 4, 5, 6, 7, 8, 9, 10 or more). Other suitable N-terminal amino acid sequences will be apparent to those skilled in the art. If X₁ lacks its own N-terminus methionine, -A- is preferably an oligopeptide (*e.g.* with 1, 2, 3, 4, 5, 6, 7 or 8 amino acids) which provides a N-terminus methionine.

-B- is an optional C-terminal amino acid sequence. This will typically be short (*e.g.* 40 or fewer amino acids *i.e.* 39, 38, 37, 36, 35, 34, 33, 32, 31, 30, 29, 28, 27, 26, 25, 24, 23, 22, 21, 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1). Examples include sequences to direct protein trafficking, short peptide sequences which facilitate cloning or purification (*e.g.* comprising histidine tags *i.e.* His_{*n*}, where *n* = 3, 4, 5, 6, 7, 8, 9, 10 or more), or sequences which enhance protein stability. Other suitable C-terminal amino acid sequences will be apparent to those skilled in the art. Most preferably, *n* is 2 or 3.

EXAMPLE 8: Active Maternal Immunization Assay using fusion proteins of Fragments of GBS 80, GBS 67, and GBS 322

In this example, fusion proteins of GBS antigens was used in the Active Maternal Immunization Assay with an isolate challenge of different GBS strains. In these experiments, the challenge dose for the different GBS strains was sufficient to kill approximately 70 – 90% of unimmunized pups and is equal to 10 x LD 50% (where LD 50% is the statistically derived Median Lethal Dose). The maternal mice were immunized according to the Active Maternal Immunization Assay schedule described above with the fusion proteins of a GBS 80 antigen with GBS 322 antigen in the GBS strains set forth in Table 14 below. Survival % was observed with the GBS fusion proteins. As shown in Table 14, in this particular challenge study, the survival rates for the fusion proteins in all of the GBS strains achieved up to 79%.

Table 14: Active Maternal Immunization Assay using fusion proteins of
GBS 80 with GBS 322

	COH1 (III)		CJB111 (V)		515 (Ia)		DK21 (II)		2603 (V)	
GBS	Dead/ treated	Survival %	Dead/ treated	Survival %	Dead/ treated	Survival %	Dead/ treated	Survival %	Dead/ treated	Survival %
80N-322	16/40	60	8/39	79	12/28	57	7/19	63	8/37	78
80	4/24	83								
PBS	35/40	12	27/35	23	32/39	18	31/40	22	33/40	17
80-322	12/27	55							12/38	68
80	0/33	100	28/40	30						
322									1/16	94
PBS	19/20	5	38/39	2	25/29	14			19/26	27

Nucleic Acids

The invention also provides nucleic acid encoding the GBS antigens and/or the hybrid fusion polypeptides of the invention. Furthermore, the invention provides nucleic acid which can hybridise to these nucleic acids, preferably under "high stringency" conditions (*e.g.* 65°C in a 0.1xSSC, 0.5% SDS solution).

Polypeptides of the invention can be prepared by various means (*e.g.* recombinant expression, purification from cell culture, chemical synthesis, *etc.*) and in various forms (*e.g.* native, fusions, non-glycosylated, lipidated, *etc.*). They are preferably prepared in substantially pure form (*i.e.* substantially free from other GAS or host cell proteins).

Nucleic acid according to the invention can be prepared in many ways (*e.g.* by chemical synthesis, from genomic or cDNA libraries, from the organism itself, *etc.*) and can take various forms (*e.g.* single stranded, double stranded, vectors, probes, *etc.*). They are preferably prepared in substantially pure form (*i.e.* substantially free from other GBS or host cell nucleic acids).

The term "nucleic acid" includes DNA and RNA, and also their analogues, such as those containing modified backbones (*e.g.* phosphorothioates, *etc.*), and also peptide nucleic acids (PNA), *etc.* The invention includes nucleic acid comprising sequences complementary to those described above (*e.g.* for antisense or probing purposes).

The invention also provides a process for producing a polypeptide of the invention, comprising the step of culturing a host cell transformed with nucleic acid of the invention under conditions which induce polypeptide expression.

The invention provides a process for producing a polypeptide of the invention, comprising the step of synthesising at least part of the polypeptide by chemical means.

The invention provides a process for producing nucleic acid of the invention, comprising the step of amplifying nucleic acid using a primer-based amplification method (e.g. PCR).

5 The invention provides a process for producing nucleic acid of the invention, comprising the step of synthesising at least part of the nucleic acid by chemical means.

Purification and Recombinant Expression

10 The GBS antigens of the invention may be isolated from *Streptococcus agalactiae*, or they may be recombinantly produced, for instance, in a heterologous host. Preferably, the GBS antigens are prepared using a heterologous host. The heterologous host may be prokaryotic (e.g. a bacterium) or eukaryotic. It is preferably *E.coli*, but other suitable hosts include *Bacillus subtilis*, *Vibrio cholerae*, *Salmonella typhi*, *Salmonella typhimurium*, *Neisseria lactamica*, *Neisseria cinerea*, *Mycobacteria* (e.g. *M.tuberculosis*), yeasts, etc.

15 Recombinant production of polypeptides is facilitated by adding a tag protein to the GBS antigen to be expressed as a fusion protein comprising the tag protein and the GBS antigen. Such tag proteins can facilitate purification, detection and stability of the expressed protein. Tag proteins suitable for use in the invention include a polyarginine tag (Arg-tag), polyhistidine tag (His-tag), FLAG-tag, Strep-tag, c-myc-tag, S-tag, calmodulin-binding peptide, cellulose-binding domain, SBP-
20 tag, chitin-binding domain, glutathione S-transferase-tag (GST), maltose-binding protein, transcription termination anti-terminiation factor (NusA), *E. coli* thioredoxin (TrxA) and protein disulfide isomerase I (DsbA). Preferred tag proteins include His-tag and GST. A full discussion on the use of tag proteins can be found at Ref. 3.

25 After purification, the tag proteins may optionally be removed from the expressed fusion protein, i.e., by specifically tailored enzymatic treatments known in the art. Commonly used proteases include enterokinase, tobacco etch virus (TEV), thrombin, and factor X_a.

GBS polysaccharides

30 The compositions of the invention may be further improved by including GBS polysaccharides. Preferably, the GBS antigen and the saccharide each contribute to the immunological response in a recipient. The combination is particularly advantageous where the saccharide and polypeptide provide protection from different GBS serotypes.

The combined antigens may be present as a simple combination where separate saccharide and polypeptide antigens are administered together, or they may be present as a conjugated
35 combination, where the saccharide and polypeptide antigens are covalently linked to each other.

Thus the invention provides an immunogenic composition comprising (i) one or more GBS polypeptide antigens and (ii) one or more GBS saccharide antigens. The polypeptide and the polysaccharide may advantageously be covalently linked to each other to form a conjugate.

Between them, the combined polypeptide and saccharide antigens preferably cover (or provide protection from) two or more GBS serotypes (*e.g.* 2, 3, 4, 5, 6, 7, 8 or more serotypes). The serotypes of the polypeptide and saccharide antigens may or may not overlap. For example, the polypeptide might protect against serogroup II or V, while the saccharide protects against either serogroups Ia, Ib, or III. Preferred combinations protect against the following groups of serotypes: (1) serotypes Ia and Ib, (2) serotypes Ia and II, (3) serotypes Ia and III, (4) serotypes Ia and IV, (5) serotypes Ia and V, (6) serotypes Ia and VI, (7) serotypes Ia and VII, (8) serotypes Ia and VIII, (9) serotypes Ib and II, (10) serotypes Ib and III, (11) serotypes Ib and IV, (12) serotypes Ib and V, (13) serotypes Ib and VI, (14) serotypes Ib and VII, (15) serotypes Ib and VIII, (16) serotypes II and III, (17) serotypes II and IV, (18) serotypes II and V, (19) serotypes II and VI, (20) serotypes II and VII, (21) serotypes II and VIII, (22) serotypes III and IV, (23) serotypes III and V, (24) serotypes III and VI, (25) serotypes III and VII, (26) serotypes III and VIII, (27) serotypes IV and V, (28) serotypes IV and VI, (29) serotypes IV and VII, (30) serotypes IV and VIII, (31) serotypes V and VI, (32) serotypes V and VII, (33) serotypes V and VIII, (34) serotypes VI and VII, (35) serotypes VI and VIII, and (36) serotypes VII and VIII.

Still more preferably, the combinations protect against the following groups of serotypes: (1) serotypes Ia and II, (2) serotypes Ia and V, (3) serotypes Ib and II, (4) serotypes Ib and V, (5) serotypes III and II, and (6) serotypes III and V. Most preferably, the combinations protect against serotypes III and V.

Protection against serotypes II and V is preferably provided by polypeptide antigens. Protection against serotypes Ia, Ib and/or III may be polypeptide or saccharide antigens.

In one embodiment, the immunogenic composition comprises a GBS saccharide antigen and at least two GBS polypeptide antigens or fragments thereof, wherein said GBS saccharide antigen comprises a saccharide selected from GBS serotype Ia, Ib, and III, and wherein said GBS polypeptide antigens comprise a combination of at least two polypeptide or a fragment thereof selected from the antigen group consisting of GBS 80, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691. Preferably, the combination includes one or more of GBS 80, GBS 104 and GBS 322. Still more preferably, the combination includes GBS 80 or a fragment thereof.

In certain embodiments, the compositions of the invention do not include a GBS polysaccharide. In certain embodiments, the combination does not include one or more of the GBS antigens selected from the group consisting of GBS 4, GBS 22, GBS 85, GBS 338 and GBS 361.

Immunogenic compositions and medicaments

Compositions of the invention are preferably immunogenic compositions, and are more preferably vaccine compositions. The pH of the composition is preferably between 6 and 8, preferably about 7. The pH may be maintained by the use of a buffer. The composition may be
5 sterile and/or pyrogen-free. The composition may be isotonic with respect to humans.

Vaccines according to the invention may either be prophylactic (*i.e.* to prevent infection) or therapeutic (*i.e.* to treat infection), but will typically be prophylactic. Accordingly, the invention includes a method for the therapeutic or prophylactic treatment of a *Streptococcus agalactiae* infection in an animal susceptible to streptococcal infection comprising administering to said animal a
10 therapeutic or prophylactic amount of the immunogenic compositions of the invention.

The invention also provides a composition of the invention for use as a medicament. The medicament is preferably able to raise an immune response in a mammal (*i.e.* it is an immunogenic composition) and is more preferably a vaccine.

The invention also provides the use of the compositions of the invention in the manufacture of
15 a medicament for raising an immune response in a mammal. The medicament is preferably a vaccine.

The invention also provides for a kit comprising a first component comprising a combination of GBS antigens.

The invention also provides a delivery device pre-filled with the immunogenic compositions of the invention.

20 The invention also provides a method for raising an immune response in a mammal comprising the step of administering an effective amount of a composition of the invention. The immune response is preferably protective and preferably involves antibodies and/or cell-mediated immunity. The method may raise a booster response.

The mammal is preferably a human. Where the vaccine is for prophylactic use, the human is
25 preferably a female (either of child bearing age or a teenager). Alternatively, the human may be elderly (e.g., over the age of 50, 55, 60, 65, 70 or 75) and may have an underlying disease such as diabetes or cancer. Where the vaccine is for therapeutic use, the human is preferably a pregnant female or an elderly adult.

30 These uses and methods are preferably for the prevention and/or treatment of a disease caused by *Streptococcus agalactiae*. The compositions may also be effective against other streptococcal bacteria.

35 One way of checking efficacy of therapeutic treatment involves monitoring GBS infection after administration of the composition of the invention. One way of checking efficacy of prophylactic treatment involves monitoring immune responses against the GBS antigens in the compositions of the invention after administration of the composition.

Compositions of the invention will generally be administered directly to a patient. Direct delivery may be accomplished by parenteral injection (*e.g.* subcutaneously, intraperitoneally, intradermally, intravenously, intramuscularly, or to the interstitial space of a tissue), or by rectal, oral (*e.g.* tablet, spray), vaginal, topical, transdermal {*e.g.* see ref. 4} or transcutaneous {*e.g.* see refs. 5 & 6}, intranasal {*e.g.* see ref. 7}, ocular, aural, pulmonary or other mucosal administration.

The invention may be used to elicit systemic and/or mucosal immunity.

Dosage treatment can be a single dose schedule or a multiple dose schedule. Multiple doses may be used in a primary immunisation schedule and/or in a booster immunisation schedule. In a multiple dose schedule the various doses may be given by the same or different routes *e.g.* a parenteral prime and mucosal boost, a mucosal prime and parenteral boost, *etc.*

The compositions of the invention may be prepared in various forms. For example, the compositions may be prepared as injectables, either as liquid solutions or suspensions. Solid forms suitable for solution in, or suspension in, liquid vehicles prior to injection can also be prepared (*e.g.* a lyophilised composition). The composition may be prepared for topical administration *e.g.* as an ointment, cream or powder. The composition may be prepared for oral administration *e.g.* as a tablet or capsule, as a spray, or as a syrup (optionally flavoured). The composition may be prepared for pulmonary administration *e.g.* as an inhaler, using a fine powder or a spray. The composition may be prepared as a suppository or pessary. The composition may be prepared for nasal, aural or ocular administration *e.g.* as drops. The composition may be in kit form, designed such that a combined composition is reconstituted just prior to administration to a patient. Such kits may comprise one or more antigens in liquid form and one or more lyophilised antigens.

Immunogenic compositions used as vaccines comprise an immunologically effective amount of antigen(s), as well as any other components, as needed. By 'immunologically effective amount', it is meant that the administration of that amount to an individual, either in a single dose or as part of a series, is effective for treatment or prevention. This amount varies depending upon the health and physical condition of the individual to be treated, age, the taxonomic group of individual to be treated (*e.g.* non-human primate, primate, *etc.*), the capacity of the individual's immune system to synthesise antibodies, the degree of protection desired, the formulation of the vaccine, the treating doctor's assessment of the medical situation, and other relevant factors. It is expected that the amount will fall in a relatively broad range that can be determined through routine trials.

Further Components of the Composition

The composition of the invention will typically, in addition to the components mentioned above, comprise one or more 'pharmaceutically acceptable carriers', which include any carrier that does not itself induce the production of antibodies harmful to the individual receiving the

composition. Suitable carriers are typically large, slowly metabolised macromolecules such as proteins, polysaccharides, polylactic acids, polyglycolic acids, polymeric amino acids, amino acid copolymers, and lipid aggregates (such as oil droplets or liposomes). Such carriers are well known to those of ordinary skill in the art. The vaccines may also contain diluents, such as water, saline, glycerol, *etc.* Additionally, auxiliary substances, such as wetting or emulsifying agents, pH buffering substances, and the like, may be present. A thorough discussion of pharmaceutically acceptable excipients is available in reference 8.

Vaccines of the invention may be administered in conjunction with other immunoregulatory agents. In particular, compositions will usually include an adjuvant.

Preferred further adjuvants include, but are not limited to, one or more of the following set forth below:

A. Mineral Containing Compositions

Mineral containing compositions suitable for use as adjuvants in the invention include mineral salts, such as aluminium salts and calcium salts. The invention includes mineral salts such as hydroxides (*e.g.* oxyhydroxides), phosphates (*e.g.* hydroxyphosphates, orthophosphates), sulphates, *etc.* (*e.g.* see chapters 8 & 9 of ref. 9)), or mixtures of different mineral compounds, with the compounds taking any suitable form (*e.g.* gel, crystalline, amorphous, *etc.*), and with adsorption being preferred. The mineral containing compositions may also be formulated as a particle of metal salt. See ref. 10.

B. Oil-Emulsions

Oil-emulsion compositions suitable for use as adjuvants in the invention include squalene-water emulsions, such as MF59 (5% Squalene, 0.5% Tween 80, and 0.5% Span 85, formulated into submicron particles using a microfluidizer). See WO90/14837. See also, Frey et al., "Comparison of the safety, tolerability, and immunogenicity of a MF59-adjuvanted influenza vaccine and a non-adjuvanted influenza vaccine in non-elderly adults", *Vaccine* (2003) 21:4234 – 4237.

Particularly preferred adjuvants for use in the compositions are submicron oil-in-water emulsions. Preferred submicron oil-in-water emulsions for use herein are squalene/water emulsions optionally containing varying amounts of MTP-PE, such as a submicron oil-in-water emulsion containing 4-5% w/v squalene, 0.25-1.0% w/v Tween 80™ (polyoxyethylsorbitan monooleate), and/or 0.25-1.0% Span 85™ (sorbitan trioleate), and, optionally, N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-*sn*-glycero-3-hydroxyphosphoryloxy)-ethylamine (MTP-PE), for example, the submicron oil-in-water emulsion known as "MF59" (International Publication No. WO 90/14837; U.S. Patent Nos. 6,299,884 and 6,451,325, incorporated herein by reference in their entireties; and Ott et al.,

"MF59 -- Design and Evaluation of a Safe and Potent Adjuvant for Human Vaccines" in *Vaccine Design: The Subunit and Adjuvant Approach* (Powell, M.F. and Newman, M.J. eds.) Plenum Press, New York, 1995, pp. 277-296). MF59 contains 4-5% w/v Squalene (e.g., 4.3%), 0.25-0.5% w/v Tween 80™, and 0.5% w/v Span 85™ and optionally contains various amounts of MTP-PE, formulated into submicron particles using a microfluidizer such as Model 110Y microfluidizer (Microfluidics, Newton, MA). For example, MTP-PE may be present in an amount of about 0-500 µg/dose, more preferably 0-250 µg/dose and most preferably, 0-100 µg/dose. As used herein, the term "MF59-0" refers to the above submicron oil-in-water emulsion lacking MTP-PE, while the term MF59-MTP denotes a formulation that contains MTP-PE. For instance, "MF59-100" contains 100 µg MTP-PE per dose, and so on. MF69, another submicron oil-in-water emulsion for use herein, contains 4.3% w/v squalene, 0.25% w/v Tween 80™, and 0.75% w/v Span 85™ and optionally MTP-PE. Yet another submicron oil-in-water emulsion is MF75, also known as SAF, containing 10% squalene, 0.4% Tween 80™, 5% pluronic-blocked polymer L121, and thr-MDP, also microfluidized into a submicron emulsion. MF75-MTP denotes an MF75 formulation that includes MTP, such as from 100-400 µg MTP-PE per dose.

Submicron oil-in-water emulsions, methods of making the same and immunostimulating agents, such as muramyl peptides, for use in the compositions, are described in detail in International Publication No. WO 90114837 and U.S. Patent Nos. 6,299,884 and 6,451,325, incorporated herein by reference in their entireties.

Complete Freund's adjuvant (CFA) and incomplete Freund's adjuvant (IFA) may also be used as adjuvants in the invention.

C. Saponin Formulations

Saponin formulations, may also be used as adjuvants in the invention. Saponins are a heterologous group of sterol glycosides and triterpenoid glycosides that are found in the bark, leaves, stems, roots and even flowers of a wide range of plant species. Saponin from the bark of the *Quillaia saponaria* Molina tree have been widely studied as adjuvants. Saponin can also be commercially obtained from *Smilax ornata* (sarsapilla), *Gypsophilla paniculata* (brides veil), and *Saponaria officianalis* (soap root). Saponin adjuvant formulations include purified formulations, such as QS21, as well as lipid formulations, such as ISCOMs.

Saponin compositions have been purified using High Performance Thin Layer Chromatography (HP-LC) and Reversed Phase High Performance Liquid Chromatography (RP-HPLC). Specific purified fractions using these techniques have been identified, including QS7, QS17, QS18, QS21, QH-A, QH-B and QH-C. Preferably, the saponin is QS21. A method of production of

QS21 is disclosed in U.S. Patent No. 5,057,540. Saponin formulations may also comprise a sterol, such as cholesterol (see WO 96/33739).

Combinations of saponins and cholesterol can be used to form unique particles called Immunostimulating Complexs (ISCOMs). ISCOMs typically also include a phospholipid such as phosphatidylethanolamine or phosphatidylcholine. Any known saponin can be used in ISCOMs. Preferably, the ISCOM includes one or more of Quil A, QHA and QHC. ISCOMs are further described in EP 0 109 942, WO 96/11711 and WO 96/33739. Optionally, the ISCOMS may be devoid of additional detergent. See ref. 11.

A review of the development of saponin based adjuvants can be found at ref. 12.

10 C. Virosomes and Virus Like Particles (VLPs)

Virosomes and Virus Like Particles (VLPs) can also be used as adjuvants in the invention. These structures generally contain one or more proteins from a virus optionally combined or formulated with a phospholipid. They are generally non-pathogenic, non-replicating and generally do not contain any of the native viral genome. The viral proteins may be recombinantly produced or isolated from whole viruses. These viral proteins suitable for use in virosomes or VLPs include proteins derived from influenza virus (such as HA or NA), Hepatitis B virus (such as core or capsid proteins), Hepatitis E virus, measles virus, Sindbis virus, Rotavirus, Foot-and-Mouth Disease virus, Retrovirus, Norwalk virus, human Papilloma virus, HIV, RNA-phages, Q β -phage (such as coat proteins), GA-phage, fr-phage, AP205 phage, and Ty (such as retrotransposon Ty protein p1). VLPs are discussed further in WO 03/024480, WO 03/024481, and Refs. 13, 14, 15 and 16. Virosomes are discussed further in, for example, Ref. 17

D. Bacterial or Microbial Derivatives

Adjuvants suitable for use in the invention include bacterial or microbial derivatives such as:

(1) *Non-toxic derivatives of enterobacterial lipopolysaccharide (LPS)*

Such derivatives include Monophosphoryl lipid A (MPL) and 3-O-deacylated MPL (3dMPL). 3dMPL is a mixture of 3 De-O-acylated monophosphoryl lipid A with 4, 5 or 6 acylated chains. A preferred "small particle" form of 3 De-O-acylated monophosphoryl lipid A is disclosed in EP 0 689 454. Such "small particles" of 3dMPL are small enough to be sterile filtered through a 0.22 micron membrane (see EP 0 689 454). Other non-toxic LPS derivatives include monophosphoryl lipid A mimics, such as aminoalkyl glucosaminide phosphate derivatives *e.g.* RC-529. See Ref. 18.

(2) *Lipid A Derivatives*

Lipid A derivatives include derivatives of lipid A from *Escherichia coli* such as OM-174. OM-174 is described for example in Ref. 19 and 20.

(3) *Immunostimulatory oligonucleotides*

Immunostimulatory oligonucleotides suitable for use as adjuvants in the invention include nucleotide sequences containing a CpG motif (a sequence containing an unmethylated cytosine followed by guanosine and linked by a phosphate bond). Bacterial double stranded RNA or oligonucleotides containing palindromic or poly(dG) sequences have also been shown to be immunostimulatory.

The CpG's can include nucleotide modifications/analogues such as phosphorothioate modifications and can be double-stranded or single-stranded. Optionally, the guanosine may be replaced with an analog such as 2'-deoxy-7-deazaguanosine. See ref. 21, WO 02/26757 and WO 99/62923 for examples of possible analog substitutions. The adjuvant effect of CpG oligonucleotides is further discussed in Refs. 22, 23, WO 98/40100, U.S. Patent No. 6,207,646, U.S. Patent No. 6,239,116, and U.S. Patent No. 6,429,199.

The CpG sequence may be directed to TLR9, such as the motif GTCGTT or TTCGTT. See ref. 24. The CpG sequence may be specific for inducing a Th1 immune response, such as a CpG-A ODN, or it may be more specific for inducing a B cell response, such as a CpG-B ODN. CpG-A and CpG-B ODNs are discussed in refs. 25, 26 and WO 01/95935. Preferably, the CpG is a CpG-A ODN.

Preferably, the CpG oligonucleotide is constructed so that the 5' end is accessible for receptor recognition. Optionally, two CpG oligonucleotide sequences may be attached at their 3' ends to form "immunomers". See, for example, refs. 27, 28, 29 and WO 03/035836.

(4) *ADP-ribosylating toxins and detoxified derivatives thereof.*

Bacterial ADP-ribosylating toxins and detoxified derivatives thereof may be used as adjuvants in the invention. Preferably, the protein is derived from *E. coli* (i.e., *E. coli* heat labile enterotoxin "LT"), cholera ("CT"), or pertussis ("PT"). The use of detoxified ADP-ribosylating toxins as mucosal adjuvants is described in WO 95/17211 and as parenteral adjuvants in WO 98/42375. Preferably, the adjuvant is a detoxified LT mutant such as LT-K63.

E. Human Immunomodulators

Human immunomodulators suitable for use as adjuvants in the invention include cytokines, such as interleukins (e.g. IL-1, IL-2, IL-4, IL-5, IL-6, IL-7, IL-12, etc.), interferons (e.g. interferon- γ), macrophage colony stimulating factor, and tumor necrosis factor.

F. Bioadhesives and Mucoadhesives

Bioadhesives and mucoadhesives may also be used as adjuvants in the invention. Suitable bioadhesives include esterified hyaluronic acid microspheres (Ref. 30) or mucoadhesives such as cross-linked derivatives of poly(acrylic acid), polyvinyl alcohol, polyvinyl pyrrolidone,

polysaccharides and carboxymethylcellulose. Chitosan and derivatives thereof may also be used as adjuvants in the invention. E.g., ref. 31.

G. Microparticles

5 Microparticles may also be used as adjuvants in the invention. Microparticles (*i.e.* a particle of ~100nm to ~150µm in diameter, more preferably ~200nm to ~30µm in diameter, and most preferably ~500nm to ~10µm in diameter) formed from materials that are biodegradable and non-toxic (*e.g.* a poly(α-hydroxy acid), a polyhydroxybutyric acid, a polyorthoester, a polyanhydride, a polycaprolactone, *etc.*), with poly(lactide-co-glycolide) are preferred, optionally treated to have a negatively-charged surface (*e.g.* with SDS) or a positively-charged surface (*e.g.* with a cationic
10 detergent, such as CTAB).

H. Liposomes

Examples of liposome formulations suitable for use as adjuvants are described in U.S. Patent No. 6,090,406, U.S. Patent No. 5,916,588, and EP 0 626 169.

I. Polyoxyethylene ether and Polyoxyethylene Ester Formulations

15 Adjuvants suitable for use in the invention include polyoxyethylene ethers and polyoxyethylene esters. Ref. 32. Such formulations further include polyoxyethylene sorbitan ester surfactants in combination with an octoxynol (Ref. 33) as well as polyoxyethylene alkyl ethers or ester surfactants in combination with at least one additional non-ionic surfactant such as an octoxynol (Ref. 34).

20 Preferred polyoxyethylene ethers are selected from the following group: polyoxyethylene-9-lauryl ether (laureth 9), polyoxyethylene-9-stearyl ether, polyoxyethylene-8-stearyl ether, polyoxyethylene-4-lauryl ether, polyoxyethylene-35-lauryl ether, and polyoxyethylene-23-lauryl ether.

J. Polyphosphazene (PCPP)

25 PCPP formulations are described, for example, in Ref. 35 and 36.

K. Muramyl peptides

30 Examples of muramyl peptides suitable for use as adjuvants in the invention include N-acetyl-muramyl-L-threonyl-D-isoglutamine (thr-MDP), N-acetyl-normuramyl-L-alanyl-D-isoglutamine (nor-MDP), and N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-*sn*-glycero-3-hydroxyphosphoryloxy)-ethylamine MTP-PE).

L. Imidazoquinolone Compounds.

Examples of imidazoquinolone compounds suitable for use as adjuvants in the invention include Imiquamod and its homologues, described further in Ref. 37 and 38.

The invention may also comprise combinations of aspects of one or more of the adjuvants identified above. For example, the following adjuvant compositions may be used in the invention:

- (1) a saponin and an oil-in-water emulsion (ref. 39);
- (2) a saponin (e.g., QS21) + a non-toxic LPS derivative (e.g., 3dMPL) (see WO 94/00153);
- (3) a saponin (e.g., QS21) + a non-toxic LPS derivative (e.g., 3dMPL) + a cholesterol;
- (4) a saponin (e.g. QS21) + 3dMPL + IL-12 (optionally + a sterol) (Ref. 40);
- (5) combinations of 3dMPL with, for example, QS21 and/or oil-in-water emulsions (Ref. 41);
- (6) SAF, containing 10% Squalane, 0.4% Tween 80, 5% pluronic-block polymer L121, and thr-MDP, either microfluidized into a submicron emulsion or vortexed to generate a larger particle size emulsion.
- (7) RibiTM adjuvant system (RAS), (Ribi Immunochem) containing 2% Squalene, 0.2% Tween 80, and one or more bacterial cell wall components from the group consisting of monophosphorylipid A (MPL), trehalose dimycolate (TDM), and cell wall skeleton (CWS), preferably MPL + CWS (DetoxTM); and
- (8) one or more mineral salts (such as an aluminum salt) + a non-toxic derivative of LPS (such as 3dPML).

Aluminium salts and MF59 are preferred adjuvants for parenteral immunisation. Mutant bacterial toxins are preferred mucosal adjuvants.

The composition may include an antibiotic.

Further antigens

The compositions of the invention may further comprise one or more additional non-GBS antigens, including additional bacterial, viral or parasitic antigens.

In another embodiment, the GBS antigen combinations of the invention are combined with one or more additional, non-GBS antigens suitable for use in a vaccine designed to protect elderly or immunocomprised individuals. For example, the GBS antigen combinations may be combined with an antigen derived from the group consisting of *Enterococcus faecalis*, *Staphylococcus aureus*, *Staphylococcus epidermis*, *Pseudomonas aeruginosa*, *Legionella pneumophila*, *Listeria monocytogenes*, *Neisseria meningitides*, influenza, and Parainfluenza virus ('PIV').

Where a saccharide or carbohydrate antigen is used, it is preferably conjugated to a carrier protein in order to enhance immunogenicity {e.g. refs. 42 to 51}. Preferred carrier proteins are bacterial toxins or toxoids, such as diphtheria or tetanus toxoids. The CRM₁₉₇ diphtheria toxoid is particularly preferred {52}. Other carrier polypeptides include the *N.meningitidis* outer membrane

protein {53}, synthetic peptides {54, 55}, heat shock proteins {56, 57}, pertussis proteins {58, 59}, protein D from *H.influenzae* {60}, cytokines {61}, lymphokines, hormones, growth factors, toxin A or B from *C.difficile* {62}, iron-uptake proteins {63}, *etc.* Where a mixture comprises capsular saccharides from both serogroups A and C, it may be preferred that the ratio (w/w) of MenA
 5 saccharide:MenC saccharide is greater than 1 (*e.g.* 2:1, 3:1, 4:1, 5:1, 10:1 or higher). Different saccharides can be conjugated to the same or different type of carrier protein. Any suitable conjugation reaction can be used, with any suitable linker where necessary.

Toxic protein antigens may be detoxified where necessary *e.g.* detoxification of pertussis toxin by chemical and/or genetic means.

10 Where a diphtheria antigen is included in the composition it is preferred also to include tetanus antigen and pertussis antigens. Similarly, where a tetanus antigen is included it is preferred also to include diphtheria and pertussis antigens. Similarly, where a pertussis antigen is included it is preferred also to include diphtheria and tetanus antigens.

15 Antigens in the composition will typically be present at a concentration of at least 1 µg/ml each. In general, the concentration of any given antigen will be sufficient to elicit an immune response against that antigen.

20 As an alternative to using protein antigens in the composition of the invention, nucleic acid encoding the antigen may be used {*e.g.* refs. 64 to 72}. Protein components of the compositions of the invention may thus be replaced by nucleic acid (preferably DNA *e.g.* in the form of a plasmid) that encodes the protein.

Definitions

The term “comprising” means “including” as well as “consisting” *e.g.* a composition “comprising” X may consist exclusively of X or may include something additional *e.g.* X + Y.

25 The term “about” in relation to a numerical value *x* means, for example, $x \pm 10\%$.

References to a percentage sequence identity between two amino acid sequences means that, when aligned, that percentage of amino acids are the same in comparing the two sequences. This alignment and the percent homology or sequence identity can be determined using software programs known in the art, for example those described in section 7.7.18 of reference 73. A preferred
 30 alignment is determined by the Smith-Waterman homology search algorithm using an affine gap search with a gap open penalty of 12 and a gap extension penalty of 2, BLOSUM matrix of 62. The Smith-Waterman homology search algorithm is disclosed in reference 74.

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WHAT IS CLAIMED IS:

1. A composition comprising a combination of two or more GBS antigens, wherein said combination includes GBS 80 or a fragment thereof or a polypeptide sequence having 50% or greater sequence identity thereto.
2. The composition of claim 1, wherein said combination of GBS antigens demonstrates improved immunogenicity as measured by the Active Maternal Immunization Assay, wherein said Active Maternal Immunization Assay measures serum titers of female mice during an immunization schedule and percent survival rate of pups after challenge.
3. The composition of claim 2, wherein the percent survival rate of challenged pups is at least 2 percentage points higher than the percent survival rate of challenged pups from female mice immunized with a single non-GBS 80 antigen.
4. The composition of claim 1, wherein said combination consists of two GBS antigens.
5. The composition of claim 1, wherein said combination consists of three GBS antigens.
6. The composition of claim 1, wherein said combination consists of four GBS antigens.
7. The composition of claim 1, wherein said combination consists of five GBS antigens.
8. The composition of claim 1, wherein GBS 80 comprises the amino acid sequence of SEQ ID NO 2 or an immunogenic fragment thereof.
9. The composition of claim 1, wherein the fragment of GBS 80 comprises the amino acid sequence selected from the group consisting of SEQ ID NOS: 3, 4, 5, 6, 7, 8, and 9.
10. The composition of claim 1, said combination consisting of two to thirteen GBS antigens selected from the group consisting of GBS 80, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691.
11. The composition of claim 1, said combination including GBS 80, GBS 104 and GBS 322.
12. The composition of claim 1, said combination including GBS 80, GBS 104, GBS 276 and GBS 322.
13. The combination of claim 1 wherein said combination comprises at least one of GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, or GBS 691.

14. A fusion protein comprising a portion of a GBS 80 antigen and a portion of at least one GBS antigen.
15. The fusion protein of claim 14 wherein said at least one GBS antigen is selected from the group consisting of GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, or GBS 691.
16. The fusion protein of claim 15 wherein said at least one GBS antigen is GBS 322.
17. The fusion protein of claim 16 consisting essentially of a GBS 80 antigen and a GBS 322 antigen.
18. A method for the therapeutic or prophylactic treatment of GBS infection in an animal susceptible to GBS infection comprising administering to said animal a therapeutic or prophylactic amount of the composition of claim 1.
19. A method for the manufacture of a medicament for raising an immune response against GBS comprising combining a GBS 80 antigen or fragment thereof with at least one GBS polypeptide antigen.
20. The method of claim 19 wherein said at least one GBS polypeptide antigen comprises a polypeptide or fragment thereof selected from the antigen group consisting of GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691.
21. Use of the compositions of any one of claims 1-17 in the preparation of a medicament for treatment of GBS infection.